No. 11690

IN THE

United States Circuit Court of Appeals

FOR THE NINTH CIRCUIT

PASADENA RESEARCH LABORATORIES, INC., a corporation, and RUSSELL R. BAVOUSET,

Appellants,

vs.

UNITED STATES OF AMERICA,

Appellee.

TRANSCRIPT OF RECORD

Upon Appeals from the District Court of the United States for the Southern District of California, Central Division

---

Parker & Company, Law Printers, Los Angeles. Phone TR. 5206.

No. 11690

IN THE

United States Circuit Court of Appeals

FOR THE NINTH CIRCUIT

PASADENA RESEARCH LABORATORIES, INC., a corporation, and RUSSELL R. BAVOUSET,

Appellants,

vs.

UNITED STATES OF AMERICA,

Appellee.

TRANSCRIPT OF RECORD

Upon Appeals from the District Court of the United States for the Southern District of California, Central Division

---

Parker & Company, Law Printers, Los Angeles. Phone TR. 5206.

INDEX

[Clerk's Note: When deemed likely to be of an important nature, errors or doubtful matters appearing in the original certified record are printed literally in italics; and likewise, cancelled matter appearing in the original certified record is printed and cancelled herein accordingly. When possible an omission from the text is indicated by printing in italics the two words between which the omission seems to occur.]

INDEX TO EXHIBITS

Government's Exhibits:

NAMES AND ADDRESSES OF ATTORNEYS:

For Appellants:

JOHN C. STICK

510 South Spring Street

Los Angeles 13, Calif.

and

R. WELTON WHANN

315 West Ninth Street

Los Angeles 15, Calif.

For Appellee:

JAMES M. CARTER

United States Attorney

ERNEST A. TOLIN

NORMAN W. NEUKOM

Assistants U. S. Attorney

600 U. S. Post Office and Court House Building

Los Angeles 12, Calif. [1*]

*Page number appearing at foot of Certified Transcript.

F. D. C. No. 21441

In the District Court of the United States for the Southern District of California
Central Division

No. 19223

UNITED STATES OF AMERICA

v.

PASADENA RESEARCH LABORATORIES, INC., a corporation, and RUSSELL R. BAVOUSET, an individual.

INFORMATION
(21 U. S. C. 331 and 333)

COUNT I

[21 U. S. C. 331(a), 333(a), 351(c)]

The United States Attorney charges:

That the Pasadena Research Laboratories, Inc., a corporation organized and existing under the laws of the State of California and trading and doing business at Pasadena, State of California, and Russell R. Bavouset, an individual, at the time hereinafter mentioned Secretary-Treasurer of said corporation, did, within the Southern District of California, on or about September 17, 1945, in violation of the Federal Food, Drug, and Cosmetic Act, unlawfully cause to be introduced and delivered for introduction into interstate commerce, at Pasadena, State of California, for delivery to Cheyenne, State of Wyoming, consigned to Dr. Joseph C. Bunten, a number of vials containing a drug;

That displayed upon said vials, when caused to be introduced and delivered for introduction into interstate

commerce as aforesaid, was the following printed and graphic matter:

30 cc Vial STERILE No. 92
INDOFORM

EACH CC CONTAINS:

Suprarenal Cortex	30 grs.	Whole Ovarian	40 grs.
Anterior Pituitary	30 grs.	Thymus Substance	15 grs.
Posterior Pituitary		Thyroid Substance	1 gr.
	3 Int'l Units	Lymphatic Substance	5 grs.

Preserved with Chlorobutanol (Chloroform Derivative) 0.5% (w/v) and Tricresol 0.5% (v/v)

This preparation does not contain any known therapeutically useful constituent.

Caution: To be used only by or on the prescription of a physician. [2]

PASADENA RESEARCH LABORATORIES, Inc.
Pasadena 8, Calif., U. S. A.

Lot No. 728

That said drug, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was then and there adulterated within the meaning of 21 U. S. C. 351(c), in that its strength differed from that which it purported and was represented to possess, in that each cubic centimeter of said drug purported and was represented to contain 3 International Units of Posterior Pituitary and 1 grain of Thyroid Substance, whereas, in fact and in truth, each cubic centimeter of said drug did not contain 3 International Units of Posterior Pituitary but did contain less than that amount of Posterior

Pituitary, and each cubic centimeter of said drug did not contain 1 grain of Thyroid Substance but did contain no Thyroid Substance.

COUNT II

[21 U. S. C. 331, 333, 352(a)]

The United States Attorney further charges:

That the Pasadena Research Laboratories, Inc., a corporation organized and existing under the laws of the State of California and trading and doing business at Pasadena, State of California, and Russell R. Bavouset, an individual, at the time hereinafter mentioned Secretary-Treasurer of said corporation, did, within the Southern District of California, on or about September 17, 1945, in violation of the Federal Food, Drug, and Cosmetic Act, unlawfully cause to be introduced and delivered for introduction into interstate commerce, at Pasadena, State of California, for delivery to Cheyenne, State of Wyoming, consigned to Dr. Joseph C. Bunten, a number of vials containing a drug;

That displayed upon said vials, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was the printed and graphic matter displayed upon the vials described in the first count of this information, which said description in said first count, is, by reference, hereby incorporated in this count; [3]

That said drug, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was then and there misbranded within the meaning of 21 U. S. C. 352(a), in that the statements, to wit, "Each CC Contains: * * * Posterior Pituitary 3 Int'l Units * * * Thyroid Substance 1 gr.", displayed on the

vials containing said drug as aforesaid, were false and misleading in this, that the said statements represented and suggested that each cubic centimeter of said drug contained 3 International Units of Posterior Pituitary and 1 grain of Thyroid Substance whereas, in fact and in truth, each cubic centimeter of said drug did not contain 3 International Units of Posterior Pituitary, but did contain less than that amount of Posterior Pituitary, and each cubic centimeter of said drug did not contain 1 grain of Thyroid Substance but did contain no Thyroid Substance.

COUNT III

[21 U. S. C. 331, 333, 351(c)]

The United States Attorney further charges:

That the Pasadena Research Laboratories, Inc., a corporation organized and existing under the laws of the State of California and trading and doing business at Pasadena, State of California, and Russell R. Bavouset, an individual, at the time hereinafter mentioned Secretary-Treasurer of said corporation, did, within the Southern District of California, on or about July 16, 1945, in violation of the Federal Food, Drug, and Cosmetic Act, unlawfully cause to be introduced and delivered for introduction into interstate commerce, at Pasadena, State of California, for delivery to Reno, State of Nevada, consigned to Dr. Clement Swaim, a number of vials containing a drug;

That displayed upon said vials, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was the following printed and graphic matter:

30 CC STERILE SOLUTION No.256

PLURI-B [4]

(Some factors of the B Complex)

For Intramuscular Use

EACH CC CONTAINS:

Thiamine Hydrochloride	50 Mgms.
Riboflavin	1 Mgm.
Pyridoxine Hydrochloride	10 Mgms.
Pantothenic Acid	10 Mgms.
Nicotinamide	50 Mgms.
Chlorobutanol (Chloroform deriv.)	1/12 gr.—0.005 gm.

CAUTION: To be used only by or on the prescription of a physician.

PASADENA RESEARCH LABORATORIES, Inc.

Pasadena 8, Calif., U. S. A.

That said drug, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was then and there adulterated within the meaning of 21 U. S. C. 351(c), in that its strength differed from that which it purported and was represented to possess, in that said drug purported and was represented to contain 50 milligrams of thiamine hydrochloride in each cubic centimeter, whereas, in fact and in truth, said drug did not contain 50 milligrams of thiamine hydrochloride in each cubic centimeter, but did contain less than that amount of thiamine hydrochloride.

COUNT IV

[21 U. S. C. 331, 333, 352(a)]

The United States Attorney further charges:

That the Pasadena Research Laboratories, Inc., a corporation organized and existing under the laws of the State of California and trading and doing business at Pasadena, State of California, and Russell R. Bavouset, an individual, at the time hereinafter mentioned Secretary-Treasurer of said corporation, did, within the Southern District of California, on or about July 16, 1945, in violation of the Federal Food, Drug, and Cosmetic Act, unlawfully cause to be introduced and delivered for introduction into interstate commerce, at Pasadena, State of California, for delivery to Reno, State of Nevada, consigned to Dr. Clement Swaim, a number of vials containing a drug; [5]

That displayed upon said vials, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was the printed and graphic matter displayed upon the vials described in the third count of this information, which said description in said third count, is, by reference, hereby incorporated in this count;

That said drug, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was then and there misbranded within the meaning of 21 U. S. C. 352(a), in that the statement, to wit, "Each CC Contains * * * Thiamine Hydrochloride—50 Mgms.", displayed on the vials containing said drug as

aforesaid, was false and misleading in this, that the said statement represented and suggested that said drug contained 50 milligrams of Thiamine Hydrochloride in each cubic centimeter whereas, in fact and in truth, said drug did not contain 50 milligrams of Thiamine Hydrochloride in each cubic centimeter, but did contain less than that amount of Thiamine Hydrochloride.

COUNT V

[21 U. S. C. 331, 333, 351(a)]

The United States Attorney further charges:

That the Pasadena Research Laboratories, Inc., a corporation organized and existing under the laws of the State of California and trading and doing business at Pasadena, State of California, and Russell R. Bavouset, an individual, at the time hereinafter mentioned Secretary-Treasurer of said corporation, did, within the Southern District of California, on or about November 19, 1945, in violation of the Federal Food, Drug, and Cosmetic Act, unlawfully cause to be introduced and delivered for introduction into interstate commerce, at Pasadena, State of California, for delivery to Sunnyside, State of Washington, consigned to Dr. C. A. Hughes, one vial containing a drug;

That displayed upon said vial, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was the following printed and graphic matter: [6]

15 CC STERILE No. 270
INJECTABLE
VITAMIN D (In Oil)
(Activated Ergosterol)
For Intramuscular Use
500,000 U. S. P. Units Per cc.
CAUTION: To be used only by or on the prescription of a physician.
PASADENA RESEARCH LABORATORIES
Pasadena 8, Calif., U. S. A.

That said drug, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was then and there adulterated within the meaning of 21 U. S. C. 351(c), in that its strength differed from that which it purported and was represented to possess, in that said drug purported and was represented to contain 500,000 U. S. P. Units of Vitamin D per cubic centimeter, whereas, in fact and in truth, said drug did not contain 500,000 U. S. P. Units of Vitamin D per cubic centimeter but did contain less than that amount of Vitamin D.

COUNT VI
[21 U. S. C. 331, 333, 352(a)]

The United States Attorney further charges:

That the Pasadena Research Laboratories, Inc., a corporation organized and existing under the laws of the State of California and trading and doing business at Pasadena, State of California, and Russell R. Bavouset, an individual, at the time hereinafter mentioned Secretary-Treasurer of said corporation, did, within the Southern District of California, on or about November 19,

1945, in violation of the Federal Food, Drug, and Cosmetic Act, unlawfully cause to be introduced and delivered for introduction into interstate commerce, at Pasadena, State of California, for delivery to Sunnyside, State of Washington, consigned to Dr. C. A. Hughes, one vial containing a drug;

That displayed upon said vial, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was [7] the printed and graphic matter displayed upon the vial described in the fifth count of this information, which said description in said fifth count, is, by reference, hereby incorporated in this count;

That said drug, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was then and there misbranded within the meaning of 21 U. S. C. 352(a), in that the statement, to wit, "Vitamin D * * * 500,000 U. S. P. Units per cc.", displayed on the vial containing said drug as aforesaid, was false and misleading in this, that the said statement represented and suggested that said drug contained 500,000 U. S. P. Units of Vitamin D per cubic centimeter whereas, in fact and in truth, said drug did not contain 500,000 U. S. P. Units of Vitamin D per cubic centimeter, but did contain less than that amount of Vitamin D.

COUNT VII

[21 U. S. C. 331, 333, 351(c)]

The United States Attorney further charges:

That the Pasadena Research Laboratories, Inc., a corporation organized and existing under the laws of the State of California and trading and doing business at Pasadena, State of California, and Russell R. Bavouset, an individual, at the time hereinafter mentioned Secre-

tary-Treasurer of said corporation, did, within the Southern District of California, on or about June 18, 1946, in violation of the Federal Food, Drug, and Cosmetic Act, unlawfully cause to be introduced and delivered for introduction into interstate commerce, at Pasadena, State of California, for delivery to Phoenix, State of Arizona, consigned to Dr. P. M. Ryerson, a number of vials containing a drug;

That displayed upon said vials, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was the following printed and graphic matter:

30 cc STERILE SOLUTION No. 256
PLURI-B [8]
(Some factors of the B Complex)
For Intramuscular or Intravenous Use

EACH CC CONTAINS:

Thiamine Hydrochloride	50 Mgms.
Riboflavin	2 Mgms.
Pyridoxine Hydrochloride	10 Mgms.
Pantothenic Acid	10 Mgms.
Nicotinamide	50 Mgms.
Chlorobutanol (Chloroform deriv.)	1/12 gr.—0.005 gm.

Caution: To be dispensed only by or on the Prescription of a physician.

Lot No. 317

PASADENA RESEARCH LABORATORIES, Inc.
Pasadena 8, Calif., U. S. A.

That said drug, when caused to be introduced and delivered for introduction into interstate commerce as aforesaid, was then and there adulterated within the meaning

of 21 U. S. C. 351(c), in that its purity and quality fell below that which it purported and was represented to possess, in that said drug purported and was represented to be a drug suitable and appropriate for intramuscular and intravenous administration, to wit, injection into the muscular tissues and veins, a use which requires a product free from undissolved material, whereas said drug was unsuitable and inappropriate for intramuscular and intravenous administration in that said drug contained undissolved material.

JAMES M. CARTER
United States Attorney for the Southern District of California
By Alfred P. Chamie
Assistant United States Attorney

[Endorsed]: Filed Mar. 18, 1947. [9]

[Minutes: Monday, April 7, 1947]

Present: The Honorable Wm. C. Mathes, District Judge.

This cause coming on for plea of defendants Pasadena Research Laboratories, Inc., a corporation, and Russell R. Bavouset; R. H. Kinnison, Assistant U. S. Attorney, appearing as counsel for the Government; John C. Stick, Esq., appearing as counsel for the defendants; Russell R. Bavouset, defendant, being present on his own recognizance, and as secretary and treasurer of the defendant corporation; defendant Russell R. Bavouset in his own behalf and that of the defendant corporation pleads not guilty to all counts of the Information.

It is ordered that the cause is hereby set for trial on June 17, 1947, at 10 A. M., before Judge Weinberger. [10]

[Title of District Court and Cause]

STIPULATION PERTAINING TO INTERSTATE SHIPMENT AND CERTAIN FACTS RELEVANT THERETO

It Is Hereby Stipulated by and between James M. Carter, United States Attorney, and Norman W. Neukom, Assistant United States Attorney, for and on behalf of the plaintiff, and John C. Stick, attorney for the defendants, as follows:

I.

That at the time of the trial of the herein action the Government need not offer any proof as to the interstate shipment of the drug or products set forth in each and every count of the herein Information; it being stipulated that the named defendants did ship or did cause to be shipped in interstate commerce, on or about the dates set forth in each of the respective counts of the Information, the drug or product herein named and described, from Los Angeles, California, to the named consignees at the location or place designated in each of the respective counts of said Information. [11]

II.

It Is Further Stipulated that there was displayed upon the vials or containers of the product or drug described in each of the counts of said Information, when caused to be so introduced and delivered in interstate commerce, labels stating substantially the printed and graphic matter as is alleged in each of the counts of said Information, either in words and figures or by reference to another count.

III.

It Is Further Stipulated that each of the designated and named consignees did receive, shortly after the date of each shipment, one or more vials or packages containing the product or drug so shipped in interstate commerce by the named defendants.

IV.

So as to shorten the time of trial and to avoid the necessity of any unnecessary testimony, It Is Further Stipulated with respect to each of the counts that the additional following factual matter is stipulated to; it being understood and agreed that if the persons named were called to the stand he would testify under oath to the following facts:

V.

(With reference to Counts One and Two)

The described product "Indoform" was shipped by the defendants on or about September 17, 1945, in interstate commerce, from Pasadena, California, to Dr. Joseph C. Bunten, Cheyenne, Wyoming, said shipment consisting of a number of vials containing a product or drug bearing, at time of said shipment, labels stating substantially the printed and graphic matter as is set out in Counts One and Two. That on or about January 24, 1946, a sample consisting of one vial and contents from said shipment was collected by Inspector Ralph M. Davidson, Federal Food and Drug Inspector, from the said Dr. Joseph C. Bunten; that the said Inspector marked and identified the label on the vial "27131 H, 1/24/46 RMD"; that he sealed the vial and contents with an official seal identified "27131 H, 1/24/46 Ralph M.

Davidson"; that the sample and contents so identified and [12] sealed was forwarded by the Inspector by U. S. Mail to Pharmacology Division, Food and Drug Administration, Washington, D. C.

VI.

(With reference to Counts Three and Four)

The described product "Pluri-B" was shipped by the defendants on or about July 16, 1945, in interstate commerce, from Pasadena, California, to Dr. Clement Swaim, 125 North Virginia, Reno, Nevada, consisting of a number of vials containing a product or drug bearing at said time on the container substantially the printed and graphic matter as is set out in Counts Three and Four. That on or about August 30, 1945, a sample consisting of two vials and contents from said shipment was obtained by Inspector Frank A. Griebling of Federal Food and Drug Administration, from the said Dr. Clement Swaim; that the said Inspector sealed the vials and contents with official seals marked and identified "29953 H, 8/30/45 Frank A. Griebling"; that the sample and contents so identified and sealed was forwarded by the Inspector, by U. S. Mail, to Vitamin Division, Food and Drug Administration, Washington, D. C.

VII.

(With reference to Counts Five and Six)

The described product "Vitamin D" was shipped by the defendants on or about November 25, 1945, in interstate commerce, from Pasadena, California, to Dr. C. A. Hughes, Sunnyside, Washington, namely, a vial containing a product or drug and bearing the label substantially

as is set out in Counts Five and Six. That on or about January 9, 1946, this vial and contents was obtained as a sample by Inspector Charles C. Cooley of Federal Food and Drug Administration, from the said Dr. C. A. Hughes; that the said Inspector identified and marked the label on the vial "58019 H, 1/9/46 CCC"; that he sealed the carton holding the vial and contents with an official seal identified "58019 H, 1/9/46 Charles C. Cooley"; that the sample and contents so identified and sealed was forwarded by the Inspector, by U. S. Mail, to Pharmacology Division, Food and Drug Administration, Washington, D. C. [13]

VIII.

(With reference to Count Seven)

The described product "Pluri-B" was shipped by the defendants on or about June 18, 1946, in interstate commerce, from Pasadena, California, to Dr. P. M. Ryerson, 1505 E. McDowell Road, Phoenix, Arizona, consisting of a number of vials containing a product or drug bearing at said time a label stating substantially the printed and graphic matter as is set out in Count Seven. That on or about July 12, 1946, Inspector Maurice P. Kerr, Federal Food and Drug Inspector, collected a sample consisting of six vials and contents, each at random from different boxes of the said shipment in the possession of Dr. P. M. Ryerson; that the said Inspector marked and identified the labels on the vials "30694 H, 7/12/46 MPK"; that he sealed the vials and contents with official seals identified "30694 H, 7/12/46 Maurice P. Kerr"; that the samples and contents so identified and sealed were forwarded by the Inspector by Railway Express to

Pharmacology Division, Food and Drug Administration, Washington, D. C.

Dated this 10 day of June, 1947.

JAMES M. CARTER
United States Attorney

NORMAN W. NEUKOM
Assistant U. S. Attorney
Chief of Criminal Division

Attorneys for Plaintiff

JOHN C. STICK

Attorney for Defendants

[Endorsed]: Filed Jun. 17, 1947. [14]

[Title of District Court and Cause]

WAIVER OF TRIAL BY JURY AND WAIVER OF SPECIAL FINDINGS OF FACT
(Rule 23(a) and (c) F. R. C. P.)

The undersigned defendant hereby waives the right to a trial by jury and requests the court to try all charges against him in this cause without a jury.

The undersigned defendant further waives the right to request any special findings of fact as provided by Rule 23(c) of the Federal Rules of Criminal Procedure.

June 17, 1947.

PASADENA RESEARCH LABS., INC.
By Russell R. Bavouset
Gen. Mgr.

RUSSELL R. BAVOUSET
Defendant

The undersigned counsellor represents that prior to the signing of the foregoing waiver, the defendant was fully advised as to the rights of an accused under the Constitution and laws of the United States, including the right to a trial by jury and the right to request special findings in a case tried without a jury; and further represents that, in his opinion, the above waiver by the defendant of trial by jury and special findings is voluntarily and understandingly made.

June 17, 1947.

JOHN C. STICK
Attorney for Defendants

The United States Attorney hereby consent that the case be tried without a jury, and waives the right to request any special findings of fact as provided by Rule 23(c) of the Federal Rules of Criminal Procedure.

June 17, 1947.

JAMES M. CARTER
United States Attorney
By Norman W. Neukom
Assistant U. S. Attorney

Approved June 17, 1947.

WM. C. MATHES
United States District Judge

[Endorsed]: Filed Jun. 17, 1947. [15]

[Minutes: Friday, June 20, 1947]

Present: The Honorable Wm. C. Mathes, District Judge.

Further trial;

Norman Neukom, Asst. U. S. Atty., appearing for the Government;

John C. Stick, Esq., appearing for the defendants;

Defendant's Exhibits A, B, C, D, and E for identification are marked in evidence at Atty. Stick's request. Witness Jike resumes his testimony. The defense rests.

Witness Tolle, heretofore sworn, testifies further. Witness Mason, heretofore sworn, testifies further. Witness Wiley, heretofore sworn, resumes his testimony. The Government rests.

At 11:52 A. M. Attorney Neukom argues for the plaintiff. At 12:20 P. M. Court recesses.

At 1:52 P. M. Court reconvenes, all being present as before, at 2:02 P. M. Attorney Stick argues for defendants. At 2:45 P. M. Attorney Neukom argues for U. S. in rebuttal.

The Court finds both defendants guilty on counts 1, 2, 3 and 7 and not guilty on counts 5 and 6 and the cause is ordered referred to the Probation Officer for report and is continued to July 7, 1947, 1:30 P. M. for sentence.

Pursuant to stipulation, it is ordered that exhibits may be returned to parties at expiration of appeal period if no appeal is taken. [16]

District Court of the United States for the
Southern District of California
Central Division

No. 19223

Criminal Information in Seven Counts for Violation of 21 U. S. C. 331(a), 333(a), 351(c)

UNITED STATES OF AMERICA

v.

PASADENA RESEARCH LABORATORIES, INC.

JUDGMENT

On this 7th day of July, 1947 came the attorney for the government and the defendant appeared in person and with John C. Stick, Esquire, its counsel.

It Is Adjudged that the defendant has been convicted upon its plea of not guilty and finding of guilty by the court, after trial without a jury, jury trial having been waived, of the offenses of transporting in interstate commerce drugs, some of which were misbranded, and others were adulterated, in that their strength was not as indicated on the labels, as charged in Counts One, Two, Three, Four and Seven of the information; and the court having asked the defendant whether it has anything to say why judgment should not be pronounced, and no sufficient cause to the contrary being shown or appearing to the Court,

It Is Adjudged that the defendant is guilty as charged and convicted.

It Is Adjudged that the defendant pay to the United States of America a fine of $1,000 for the offense charged in the First Count of the information; and a fine of $1,000 for the offense charged in the Second Count of the information; and a fine of $1,000 for the offense charged in the Third Count of the information; and a fine of $1,000 for the offense charged in the Fourth Count of the information; and a fine of $1,000 for the offense charged in the Seventh Count of the information.

It Is Further Adjudged that payment of a single fine of $1,000 shall satisfy the fines imposed under Counts One and Two of the information; and that a single fine of $1,000 shall satisfy the fines imposed under Counts Three and Four of the information; and that payment of a total fine of $3,000 shall fully satisfy and discharge all fines imposed under Counts One, Two, Three, Four and Seven.

It is Adjudged that the defendant is not guilty of the offenses charged in Counts Five and Six of the information.

It Is Further Adjudged that execution of this judgment be stayed until 12 o'clock noon on July 14, 1947.

WM. C. MATHES
United States District Judge

[Endorsed]: Filed Jul. 7, 1947. [17]

District Court of the United States for the
Southern District of California
Central Division

No. 19223

Criminal Information in Seven Counts for Violation of 21 U. S. C. 331(a), 333(a), 351(c)

UNITED STATES OF AMERICA

v.

RUSSELL R. BAVOUSET

PROBATIONARY ORDER

On this 7th day of July, 1947 came the attorney for the government and the defendant appeared in person and with his counsel John C. Stick, Esquire.

It Is Adjudged that the defendant has been convicted upon his plea of not guilty and finding of guilty by the court, after trial without a jury, jury trial having been waived, of the offenses of transporting in interstate commerce drugs, some of which were misbranded, and others adulterated, in that their strength was not as indicated on the labels, as charged in Counts One, Two, Three, Four and Seven of the information; and the court having asked the defendant whether he has anything to say why judgment should not be pronounced, and no sufficient cause to the contrary being shown or appearing to the Court,

It Is Adjudged that the defendant is guilty as charged and convicted.

It Is Adjudged that imposition of sentence for the offenses charged in Counts One, Two, Three, Four and

Seven of the information be and is hereby suspended, and the defendant is placed on probation for the period of five years commencing forthwith; and the conditions of probation are fixed as follows: during the probationary period the defendant shall (1) donate $5 or more each month from his personal earnings to a charity of his own choice, approved by the Probation Officer of this Court; (2) obey all laws applicable to his conduct; and (3) comply with all rules which the Probation Officer of this Court shall prescribe for the guidance of his personal conduct.

It Is Further adjudged that the probationary periods and the conditions of probation shall be the same as to the First, Second, Third, Fourth and Seventh Counts; that the probationary periods shall commence and run concurrently; that compliance with the conditions of probation as to the First Count shall also constitute compliance with the conditions of probation as to the Second, Third, Fourth and Seventh Counts; and that a violation of any of the conditions of probation as to the First Count shall likewise constitute a violation of the conditions as to the Second, Third, Fourth and Seventh Counts.

It Is Further Adjudged that the defendant is not guilty of the offenses charged in Counts Five and Six of the information.

WM. C. MATHES
United States District Judge

[Endorsed]: Filed Jul. 7, 1947. [18]

[Title of District Court and Cause]

NOTICE OF APPEAL BY DEFENDANT PASADENA RESEARCH LABORATORIES, INC., A CORPORATION

Name and address of appellant: Pasadena Research Laboratories, Inc., 2107 East Villa, Pasadena, California.

Name and address of appellant's attorneys: John C. Stick, 510 S. Spring Street, Los Angeles 13, California, and R. Welton Whann, 315 West Ninth Street, Los Angeles 15, California.

Offenses: Violation of the Federal Food, Drug and Cosmetic Act by misbranding and adulteration of drugs in violation of 21 U. S. C. 331(a), 351(c) and 352(a). [19]

Concise statement of judgment giving date and sentence: Defendant-appellant, Pasadena Research Laboratories, Inc., was found guilty on Counts 1, 2, 3, 4 and 7 of the information, and in the Judgment dated July 7, 1947, was sentenced to pay a fine of Three Thousand ($3,000.00) Dollars, which fine of Three Thousand ($3,000.00) Dollars has been paid.

Defendant-appellant Pasadena Research Laboratories, Inc., does hereby appeal to the United States Circuit Court of Appeals for the Ninth Circuit from the above-stated judgment.

Dated: July 16, 1947.

PASADENA RESEARCH LABORATORIES, INC.,
a corporation

By Russell R. Bavouset
Secretary-Treasurer

Defendant.

JOHN C. STICK
R. WELTON WHANN
Attorneys for Defendant-Appellant
Pasadena Research Laboratories, Inc.

Received copy of the above Notice of Appeal this 16 day of July, 1947. United States Attorney for the Southern District of California. By Norman W. Neukom, Asst. U. S. Attorney.

[Endorsed]: Filed Jul. 16, 1947. [20]

[Title of District Court and Cause]

NOTICE OF APPEAL BY DEFENDANT RUSSELL R. BAVOUSET, AN INDIVIDUAL

Name and address of appellant: Russell R. Bavouset, 2524 S. Sycamore, Los Angeles 16, California.

Name and address of appellant's attorneys: John C. Stick, 510 S. Spring Street, Los Angeles 13, California, and R. Welton Whann, 315 West Ninth Street, Los Angeles 15, California.

Offenses: Violation of the Federal Food, Drug and Cosmetic Act by misbranding and adulteration of drugs in violation of 21 U. S. C. 331(a), 351(c) and 352(a).

Concise statement of judgment giving date and sentence: Defendant-appellant Russell R. Bavouset was found guilty on [21] Counts 1, 2, 3, 4 and 7 of the information, and in the Judgment dated July 7, 1947, imposition of sentence was suspended and the defendant-appellant Russell R. Bavouset was placed on probation for a period of five (5) years under the conditions set forth in the probationary order dated July 7, 1947.

Defendant-appellant Russell R. Bavouset, does hereby appeal to the United States Circuit Court of Appeals for the Ninth Circuit from the above-stated judgment.

Dated: July 16, 1947.

RUSSELL R. BAVOUSET
an individual
Defendant

JOHN C. STICK
R. WELTON WHANN
Attorneys for Defendant-Appellant
Russell R. Bavouset

Received copy of the above Notice of Appeal this 16 day of July, 1947. United States Attorney, Southern District of California. By Norman W. Neukom, Asst. U. S. Attorney.

[Endorsed]: Filed Jul. 16, 1947. [22]

[Title of District Court and Cause]

ASSOCIATION OF ATTORNEY

R. Welton Whann is hereby associated with John C. Stick as attorney for defendants in the above-entitled cause.

JOHN C. STICK

We, Pasadena Research Laboratories, Inc., and Russell R. Bavouset, the above-named defendants, do hereby consent to and approve of the above association of attorney.

PASADENA RESEARCH LABORATORIES, INC.,
a corporation

By Russell R. Bavouset
Secretary-Treasurer

RUSSELL R. BAVOUSET
an individual [23]

I, R. Welton Whann, hereby accept the above association.

R. WELTON WHANN

Receipt of a copy of the above association of attorneys is hereby acknowledged this 16 day of July, 1947. United States Attorney for the Southern District of California. By Norman W. Neukom, Asst.

[Endorsed]: Filed Jul. 16, 1947. [24]

[Title of District Court and Cause]

STIPULATION AND ORDER FOR TRANSMISSION OF ORIGINAL PAPERS AND EXHIBITS

It Is Hereby Stipulated and Agreed, by and between the parties hereto that the Court may, if it approves, enter an order herein in the form provided for below.

Dated: Los Angeles, California, this 20 day of August, 1947.

JAMES M. CARTER
United States Attorney

RAY H. KINNISON
Assistant United States Attorney

Attorneys for Plaintiff

JOHN C. STICK
R. WELTON WHANN
By R. Welton Whann

Attorneys for Defendants [28]

It appearing that it is desirable that certain original papers and exhibits on file in the above cause should be inspected by the Circuit Court of Appeals for the Ninth Circuit, notice of appeal to that Court having been filed in this cause,

It Is Hereby Ordered, pursuant to Rule 75(i) of the Rules of Civil Procedure, that the Clerk of this Court forward, all costs thereof to be paid by Pasadena Research Laboratories, Inc. and Russell R. Bavouset, defendants-appellants, to the Clerk of the Circuit Court of Appeals for the Ninth Circuit, all original papers and other exhibits, said papers and exhibits to be held by the Clerk of the Appellate Court pending the appeal, and to be returned to the Clerk of this Court unless otherwise provided by the rules of said Appellate Court.

Dated at Los Angeles, California, this 20 day of August, 1947.

JACOB WEINBERGER
United States District Judge

[Endorsed]: Filed Aug. 20, 1947. [29]

[Title of District Court and Cause]

CERTIFICATE OF CLERK

I, Edmund L. Smith, Clerk of the District Court of the United States for the Southern District of California, do hereby certify that the foregoing pages numbered from 1 to 29, inclusive, contain full, true and correct copies of Information; Minute Order Entered April 7, 1947; Stipulation Pertaining to Interstate Shipment and Certain Facts Relevant Thereto; Waiver of Trial by Jury and of Special Findings of Fact; Minute Order Entered June 20, 1947; Judgment as to Defendant Pasadena Research Laboratories, Inc.; Probationary Order as to Defendant Russell R. Bavouset; Notice of Appeal as to each of the Defendants; Association of Attorney; Designation of Record on Appeal and Stipulation and Order for Transmission of Original Exhibits which, together with the Original Exhibits and copy of Reporter's Transcript, transmitted herewith, constitute the record on appeal to the United States Circuit Court of Appeals for the Ninth Circuit.

I further certify that my fees for preparing, comparing, correcting and certifying the foregoing record amount to $8.20 which sum has been paid to me by appellants.

Witness my hand and the seal of said District Court this 20th day of August, 1947.

(Seal) EDMUND L. SMITH
Clerk

By Theodore Hocke
Chief Deputy Clerk

[Title of District Court and Cause]

REPORTER'S TRANSCRIPT OF PROCEEDINGS

Los Angeles, California, Tuesday, June 17, 1947

Appearances:

For the Plaintiff: James M. Carter, Esq., United States Attorney; by Norman W. Neukom, Esq., Asst. U. S. Attorney.

For the Defendants: John C. Stick, Esq., and Eugene M. Ellison, Esq.

* * * * * * * * *

[Mr. Neukom made an opening statement on behalf of the plaintiff.] [2*]

* * * * * * * * *

FRANK H. WILEY,

called as a witness by the plaintiff, being first sworn, was examined and testified as follows:

The Clerk: Please state your name.

The Witness: Frank H. Wiley, W-i-l-e-y.

Direct Examination

By Mr. Neukom:

The clerk will please mark a box containing a group of bottles and a piece of paper containing attached to it some labels. Will this be either 1 or 2? It all involves one item, Count VII. [7]

The Clerk: This wrapped box, partly opened, marked Sample No. 30694-H, will be Government's 1 for iden-

*Page number appearing at top of page of original Reporter's Transcript.

(Testimony of Frank H. Wiley)

tification. The paper bearing the labels, among other words, contains the word "Pluri-B" twice, once on each label, and in the right-hand corner the number "256" will be Government's 2 for identification.

Q. By Mr. Neukom: Mr. Wiley, what is your business or occupation?

A. I am chief of the chemical section of the medical division of the Food and Drug Administration, Washington, D. C.

Q. You were so employed for about how long?

A. Since January 3, 1939.

Q. I call you "doctor." Will you please relate to the court, is that a degree in what?

A. That is a degree in biochemistry.

Q. Briefly, state your qualifications to the court.

A. I received a Bachelor and Master's degree from the University of Denver in 1925 and '26, respectively, then spent one year in a graduate school at the University of Illinois, and then three years in graduate school at the University of Michigan, where the degree of Doctor of Philosophy and Biological Chemistry was conferred upon me. I then spent about five years in research in the department of medicine at the University Hospital at Ann Arbor, Michigan. I was then [8] employed by the E. I. DuPont de Nemours Company for about five years, a little over five years, as biochemist in their institute of industry toxicology and, since January 3, 1939 I have been employed by the Food and Drug Administration.

Q. In the course of your duties did you have occasion to receive Government's Exhibit No. 1, a box containing a certain group of vials. Will you please inspect it and

(Testimony of Frank H. Wiley)

say if you see any identification of the markings of your initials or otherwise?

A. Yes; I did receive this box.

Q. You received it on or about what date?

A. If I may refer to my notes, I think my testimony might be more accurate.

Q. Yes; you may refer to your notes.

A. (After referring to notes.) I received this sample on July 23, 1946.

Q. And it had been mailed to you by one of the Food and Drug inspectors?

A. Yes; it had been mailed to the Food and Drug Administration in Washington by Inspector Kerr.

Q. Who opened the box? A. I opened the box.

Q. And you found it contained?

A. I found it contained six vials, six rubber- [9] stoppered vials, each bearing an official Food and Drug Administration seal. That seal was identified simply as being "sample 30694-H" and bore the date "7-12-46" and the name "Morris P. Kerr."

Q. The inspector? A. The inspector; yes sir.

Q. And did each of the vials have upon them a label?

A. Yes; to each vial was attached a label.

Q. Pasted upon it? A. Yes.

Q. I show you Government's Exhibit 2 for identification to which there seems to be appended two labels.

(Testimony of Frank H. Wiley)

Were those two of the labels that were on two of the six bottles?

A. These are two of the labels that were on the six bottles, that were removed in the course of the examination and I prepared them on this sheet.

Q. Now, when you first looked at these vials, the two that we have here, what happened to the other four?

A. Two of the vials were subsequently used by our division of micro-biology in a test of sterility; two of the vials were used by our department of pharmacology in testing for pyrogen.

Q. The two vials that are here as part of Government's Exhibit 1, did they remain closed as they are now?

A. Yes; they did. These vials are in the condition [10] in which I received them.

Q. Did you observe when you first received these vials and did you put them up to a light and observe whether or not they contained undissolved particles?

A. I did.

Q. Just briefly relate what you found.

Q. I found that both vials, or all six vials, as a matter of fact, were very badly contaminated with undissolved material; that is, they contained quite a quantity of material which was not in solution.

The Court: Did you see that with the naked eye?

The Witness: Yes.

(Testimony of Frank H. Wiley)

Mr. Neukom: I would like to offer into evidence Government's Exhibit 1 and pass to the court for observation the two vials in question.

The Clerk: 1 for identification in evidence.

The Court: Government's Exhibit 1 for identification is received into evidence.

Mr. Neukom: I would like to offer Government's 2 into evidence, which were the labels that were on two of the vials.

The Court: Exhibit 2 for identification received into evidence.

[GOVERNMENT'S EXHIBIT NO. 2]

30 cc STERILE SOLUTION No. 256
PLURI-B

(Some factors of the B Complex)
For Intramuscular or Intravenous Use

EACH CC CONTAINS:

Thiamine Hydrochloride	50 Mgms.
Riboflavin	2 Mgms.
Pyridoxine Hydrochloride	10 Mgms.
Pantothenic Acid	10 Mgms.
Nicotinamide	50 Mgms.

Chlorobutanol (Chloroform deriv.) 1/12 gr.—0.005 Gm.

CAUTION: To be dispensed only by or on the prescription of a physician.

PASADENA RESEARCH LABORATORIES, Inc.
Pasadena 8, Calif., U. S. A.

Lot No. 317

[Written]: #4 30694 H 7/12/46 MPK

(Government's Exhibit No. 2)

30 cc STERILE SOLUTION No. 256
PLURI-B

(Some factors of the B Complex)

For Intramuscular or Intravenous Use

EACH CC CONTAINS:

Thiamine Hydrochloride	50 Mgms.
Riboflavin	2 Mgms.
Pyridoxine Hydrochloride	10 Mgms.
Pantothenic Acid	10 Mgms.
Nicotinamide	50 Mgms.

Chlorobutanol (Chloroform deriv.) 1/12 gr.—0.005 Gm.

CAUTION: To be dispensed only by or on the prescription of a physician.

PASADENA RESEARCH LABORATORIES, Inc.
Pasadena 8, Calif., U. S. A.

Lot No. 317

[Written]: #5 30694 H 7/12/46 MPK

[Written]: U S 2 for ident. 30694-H 8-1-46 F.H.W.

Case No. 19223 Cr. U. S. vs. Pasadena Research Laboratories, etc. U. S. Exhibit 2. Date 6/17/47. No. 2 in Evidence. Clerk, U. S. District Court, Sou. Dist. of Calif. Louis J. Somers, Deputy Clerk.

No. 11690. United States Circuit Court of Appeals for the Ninth Circuit. Filed Aug. 25, 1947. Paul P. O'Brien, Clerk.

(Testimony of Frank H. Wiley)

The Clerk: So marked.

Mr. Neukom: Would your Honor like to have me hand you the vials now? [11]

The Court: Yes; if you will.

Q. By Mr. Neukom: Are you acquainted with the authority known as "Pharmacopoeia of the United States, twelfth edition"? A. I am.

Q. Are your views in accord with the views expressed in this authority with regard to the appearance of solutions or suspensions in sterile solutions? A. Yes.

Q. Is this book that I have referred to, edition No. 12, is that a standard work? A. It is.

Q. As a matter of fact it is recognized in the Food and Drug Act, is it not? A. That is true.

Mr. Neukom: I call your Honor's attention to many definitions in the Food and Drug Act, reference is had to the Pharmacopoeia.

Q. Is it the views of chemists in your position that the product or sterile solution for intravenous and intramuscular usage should or should not contain undissolved material?

A. I think perhaps such a conclusion would be outside of the field of responsibility of a chemist.

Q. I see. Are there further observations that you had [12] to make with regard to these two vials, or as to Government's Exhibit No. 1 as a result of your tests?

A. Shortly before coming to Los Angeles for this case, I re-examined the vials and found that they were still in about the same condition as regards the amount of undissolved material present.

Q. May I ask you about that? Pause at this point. Were the vials, when you examined them as of the date

(Testimony of Frank H. Wiley)

they were received, did they contain virtually the same amount of undissolved materials as they do now?

A. Yes. The amount of undissolved material there is about the same as it was when I originally examined it.

Q. In other words, it has not increased in any appreciable amount here as to your knowledge?

A. No.

Q. Do you have an opinion as to whether or not this undissolved material, as noted in this solution, was there at or about the date of June the 18, 1946, which was some several months, I believe—how long was it before you examined it?

A. The date of shipment was June 17th.

Q. June the 18th, 1946. And you examined it about—"

A. I examined it on August 1st; so that would be about six weeks before I examined it.

Q. Do you have an opinion as to whether that undissolved [13] material was present as of the date June 18, 1946? A. Yes. I—

Mr. Stick: Just a moment, your Honor. We object to that question, even though this man is an expert, unless it is shown as to what conditions this bottle was kept in or these vials, whether they were subject to any outside influences which could have affected them, whether the labels had been removed or whether anything had been done to change the condition of the solutions that were in the bottles between the time it was shipped and the time this gentleman saw them.

The Court: He testified that the bottle was sealed, did he not?

(Testimony of Frank H. Wiley)

Mr. Stick: It was sealed at the time it was picked up by the inspector on July 12th. This product was shipped June 18th, and between June 18th and July 12th, when it was picked up by the inspector, we have no evidence as to the conditions surrounding it, how long the inspector kept it and how and under what conditions it went back to Washington so that this man saw it on July 26th. We have no circumstances or no facts.

The Court: Well, strictly speaking, I suppose it would be necessary to have one of these original bottles opened by a chemist appointed by the court and have that chemist make a very minute analysis of the contents, and then express [14] his opinion as to whether or not that combination of substances in the bottle under those conditions would change in time, or whether there would be some precipitation inside the bottle or some other changes.

Mr. Stick: Yes. And also, that no outside influence of any kind affected the contents of that bottle; and that can only be determined by the evidence of the parties who had control of the bottle between the time when it was analyzed and the time when this gentleman received it and the time it was put in interstate commerce.

The Court: Well, of course, we have a bottle here which is said to be the original container. We have two of them in Exhibit 1 which are said to be original.

Mr. Neukom: They are still sealed, never been opened. I believe that is your testimony?

The Court: Unopened bottles.

Mr. Stick: That does not necessarily mean that the contents of that bottle cannot be affected.

The Court: No. My observation is this: It seems to me that, before anyone could express an opinion, he

(Testimony of Frank H. Wiley)

would have to take the contents of one of these bottles, it would have to be opened, he would have to say that he opened it, took the contents out and made an analysis, or did whatever was necessary to reach an informed opinion as an expert upon when that sediment or undissolved material came into [15] being, whether it was precipitated early or late, or whether it was in solution at the time it was placed in the bottle. I take it that a chemist can do that. I don't know.

But, can we take this witness' opinion, Mr. Neukom, based upon his examination of a bottle which had been opened and conceivably might have been tampered with or even the entire contents changed before he received it?

Mr. Neukom: Well, if that was the rule of law, you could never prosecute under the Food and Drug Act.

The Court: Oh, yes. Yes; you can take that bottle there, and the court will appoint a chemist if the counsel insists upon that type of proof. The court will appoint a chemist and the chemist can make the analysis, and we will give him the time that is necessary and he can come and express an opinion as to the contents of that bottle with respect to whatever is in there insoluble.

Mr. Neukom: Of course, my position is—may I express my opinion briefly?

The Court: Yes.

Mr. Neukom: Dr. Wiley tells me, and I believe that this would be his testimony, that he can form an opinion from observing this motherly matter or undissolved particles at the time he saw it six weeks after shipment, without even opening the bottle.

(Testimony of Frank H. Wiley)

The Court: If he can express an opinion as to one of [16] these bottles in Exhibit 1, that is a different matter.

Mr. Neukom: I understand he can express an opinion.

The Court: Suppose you inquire as to that opinion.

Mr. Neukom: Dr. Wiley—

Mr. Stick: My objection, then, is overruled?

The Court: Your objection is sustained to the question pending.

Mr. Stick: All right.

Q. By Mr. Neukom: Dr. Wiley, taking the two vials, part of Government's Exhibit No. 1, which I understand you examined about six weeks after the shipment in question here, from your knowledge of sterile solutions and from your observation of sterile solutions, your experience, are you able to express an opinion to this court as to whether or not the contents of those two vials, Government's Exhibit 1, did contain the undissolved particles you noticed there then as of the date they were shipped, namely, on or about June 18, 1946? Your answer is yes or no. A. Yes. [17]

* * * * * * * * *

Mr. Stick: He has an opinion.

Q. By Mr. Neukom: Now, waiting for the objection, what is your opinion?

Mr. Stick: I object to that, your Honor, upon the ground that until the conditions under which these bottles have existed or to which these bottles and contents have been subjected since the date that they were put into interstate commerce on June 18th must be before this witness before he can express an opinion as to whether

(Testimony of Frank H. Wiley)

or not the contents that are in there now were in the condition that it is now, going back to June 18th when it was shipped.

The Court: That may be so, Mr. Stick, but he says he has an opinion, and he says he has never opened that bottle. That is up to the experts. He can express an opinion. What you say may go to the weight of it, but not to the competency of it, I take it. Objection overruled.

Q. By Mr. Neukom: Will you please relate your opinion?

A. From experience with these materials and from general information of so-called supersaturated solutions, of which this is an example, I would say that this undissolved material was undoubtedly present on June 18th when the material was shipped. There is only one external factor of which I know that would hasten or increase the crystalization of this material, and that would be refrigeration. [18] I doubt very much if the mail bag in which this material was transmitted to Washington was in a refrigerator car.

Q. Then, in other words, coolness of, say, slightly above freezing, the temperature of the usual refrigerator, might hasten the cloudy condition?

A. It might hasten it if the crystalization had not already taken place.

Q. Normal temperatures—now, for instance, assuming that this product went where it became quite warm, and by that I will say up to 110 or 115, in your opinion, if it was sealed in those bottles here, would that have hastened the accumulation of the undissolved particles?

A. No; it would not.

(Testimony of Frank H. Wiley)

Q. Would it have any effect at all, in your opinion?

A. It might even have slowed up the appearance of those particles slightly, due to the increase of solubility at a higher temperature.

Q. In other words, heat retard and coolness might hasten? A. That is right.

Q. I call to your attention, although I believe this is evidence, maybe, your Honor, in looking at the label did you note any caution as to how it should be retained or kept with regard to heat or cold?

A. There is no caution on this label as to conditions [19] under which the product should be stored.

Q. And, Dr. Wiley, a brown bottle such as that is in is a bottle that is proper to use, is it not, in retaining solutions?

A. Yes; this type of bottle is often used for the packaging of materials that are sensitive to the light.

Q. Or blue; it is to keep out unnecessary light, isn't that it? A. That is it. That is true.

Mr. Neukom: That will be all.

The Court: The container in which that solution is found now is a proper container for the shipment of a sterile solution?

The Witness: Yes. Yes; it is a proper container.

Cross Examination

By Mr. Stick:

Q. Dr. Wiley, isn't it true that thiamin solutions, thiamine hydrochloride, have a tendency to precipitate?

A. It depends entirely upon the composition of your thiamin solution. If the thiamin used is not pure, there might be some impurities in the thiamin which will pre-

(Testimony of Frank H. Wiley)

cipitate out. However, a pure grade of thiamine hydrochloride will form a pure solution and remain clear.

Q. You spoke in your examination of a supersaturated [20] solution. What do you mean by that?

A. It is a solution which contains more of the material dissolved in the solvent than it would ordinarily hold; that is, materials are said to be soluble to the extent of so many grams per cubic centimeter. If you dissolve more material than that number of grams in a cubic centimeter of the solvent, the solution is said to be supersaturated.

Q. Was this a supersaturated solution in the vials that you have before you?

A. It was supersaturated in that it contained more riboflavin than you could ordinarily dissolve in that amount of fluid.

Q. Is riboflavin stable as to its remaining in solution?

A. If the amount dissolved is below the saturation point, I would say it was.

Q. With the formula that appears on these bottles, would you say that the thiamin and the riboflavin would have a tendency to precipitate?

A. The riboflavin would. I do not recall just how much thiamin there was in there or what the solubility of thiamin is at the moment.

Q. I will show you Government's Exhibit 2 for identification. Could you tell from looking at that? [21]

A. If you would permit me to refer also to USP to find the solubility of thiaminechloride, I think I could. (After examining data.) The label indicates that this preparation contains 50 milligrams of thiaminehydrochlride per cc; that is 5/100ths of a gram. United States

(Testimony of Frank H. Wiley)

Pharmacopoeia states that one gram of thiamine hydrochloride will dissolve in one cc of water. In other words, this preparation contained only about 1/20th of the amount of thiamine hydrochloride which you can dissolve in water, consequently it was not. If it was pure, thiaminehydrochloride don't precipitate out.

Q. Would the fact that other ingredients were dissolved in the same cubic centimeter of the contents have to do with its saturation?

A. That depends entirely upon the nature of the ingredients, of course.

Q. From the ingredients that are set forth in that formula?

A. I do not believe that the ingredients set forth on this label would cause the thiamine hydrochloride dissolved in this amount of water to precipitate.

The Court: By "this label" you are referring to Exhibit 2?

The Witness: Exhibit 2; yes.

Q. By Mr. Stick: All right. Now, what about [22] riboflavin?

A. The label in Exhibit 2 indicates that each cubic centimeter of this preparation contains two milligrams of riboflavin per cc. Riboflavin is soluble in water to the extent of about 1/10th of a milligram per cc. In other words, this solution is labeled to contain 20 times

(Testimony of Frank H. Wiley)

as much riboflavin as you can ordinarily dissolve in one cc of water.

Q. And that would have a tendency, then, to precipitate, would it not? A. It would; yes.

The Court: Did I understand you correctly that two milligrams of riboflavin in one cc of water would be approximately 20 times too much that which would dissolve in that quantity of water?

The Witness: That is 20 times as much as you could normally get in one cubic centimeter of water; yes. It might be possible to get that amount of riboflavin in water by heating it up and dissolving it. I am not sure exactly what the solubility of riboflavin at high temperatures is, but at room temperature that is 20 times the amount you would expect to stay in solution.

The Court: You would call that 20 times over-saturation?

The Witness: Yes; it could be called that.

Mr. Stick: That is all. [23]

Mr. Neukom: That is all, Doctor.

Mr. Stick: Pardon me. Your Honor, may I ask him just one more question?

Q. You did not see these vials until you saw them in Washington, is that right? A. That is true.

Q. You never saw any of them prior to that time?

A. No.

Mr. Stick: That is all.

Mr. Neukom: Dr. Thienes, please.

CLINTON H. THIENES,

called as a witness by plaintiff, being first sworn, was examined and testified as follows:

The Clerk: Please state your name.

The Witness: Clinton H. Thienes, T-h-i-e-n-e-s.

Direct Examination

By Mr. Neukom:

Q. Do you live in Los Angeles? A. Yes, sir.

Q. And your occupation?

A. I am a physician and I am also a professor of pharmacology at the University of Southern California medical school. [24]

Q. You are a graduate of what university or universities?

A. I have degrees Bachelor of Arts, Master of Arts, and Doctor of Medicine from the University of Oregon, and Doctor of Philosophy from Stanford University.

Q. You have how long been affiliated in the capacity that you have related with the University of Southern California, pharmacology?

A. I have been with the University of Southern California since 1929 and head of the Department of Pharmacology since 1931.

Q. And you are likewise practicing your profession here in the city? A. Yes; I am.

Q. Are you a member of any scientific societies, Doctor, medical societies?

A. I am a member of the American Society for Pharmacology and Experimental Therapeutics, of the Society for Experimental Biology in medicine, of the American Association for Advancement of Science, the American Medical Association, and the Los Angeles

(Testimony of Clinton H. Thienes)

Medical Association, the California Medical Association, Western Association of Industry, Physicians and Surgeons.

Q. You are not employed by the Federal Food and Drug, of course? [25] A. No; I am not.

Q. You have been retained as an expert in this case?

A. That is right.

Q. Doctor, are you familiar with the usage of sterile solutions for intramuscular or intravenous use as to their condition? Are you familiar with such solutions?

A. Yes.

Q. I will show you two vials from Government's Exhibit No. 1, and would like to ask you to put those up to the light and observe what you can see of the contents. Before doing that, Doctor, when a solution is injected into a person, it either goes into a muscular tissue or into a blood vein; isn't that true?

A. Or into the skin or just under the skin.

Q. But it can go into the blood vein, can it not?

A. That is right.

Q. And sterile solutions of such character as that—have you seen the formula of this product here?

A. I don't think I have.

Q. Will you look at Government's Exhibit No. 2?

A. These represent labels from two separate bottles of some type of preparation, I take it?

Q. Yes; that is my understanding of the testimony. They are both the same, I think, the two.

A. Yes. [26]

Q. Is such a solution, or a solution of materials, drugs, or whatever they are of that type, is that such

(Testimony of Clinton H. Thienes)

that might be used where it was injected in the blood stream? A. Yes.

Q. I note that the label says "for intravenous use."

A. Yes; and preparations of this general composition are used intravenously and intramuscularly.

Q. Doctor, you have examined the two vials there. Did you observe anything unusual?

A. There was considerable precipitate or undissolved material.

Q. In your opinion as a medical man, Doctor, would a solution containing undissolved material such as that be considered proper by physicians who adhere to the usual degree of care and caution, to use intravenously upon a human being? A. No; I would not.

Q. Doctor, if you were to inject into a person a solution which contains cloudy or undissolved particles such as you observe there, might there be any harm or any blockage of either the heart or blood stream if such particles clotted in some of the veins?

A. Particles of the size which I observe in these two vials are of sufficient size to block the smaller veins and capillaries. Some of these particles are large enough to block what we might call a fair-sized vein. [27]

Q. Might that cause harm?

A. And if injected as ordinarily injected, it would lodge in veins of the lung or, rather, in branches of the supplementary artery and cause blockage of the circulation in two parts of the lung. That might result in shock from just the sudden blocking of the vessel, and pain and subsequent infection may occur in such places.

(Testimony of Clinton H. Thienes)

Q. In your opinion would such a solution be proper—I think you did express an opinion.

A. No; such a solution would not be proper for intravenous injection.

Q. How about intramuscular?

A. It would not be proper for intramuscular injection.

The Court: Would the infection result from loss of blood supply?

The Witness: Well, from the loss of blood supply, the irritation set up. Primarily, the loss of blood supply reducing the resistance of the tissue.

Q. By Mr. Neukom: Doctor, would you expect and is it the consensus of opinion of practitioners who use intravenous or intramuscular solutions, sterile solutions, that such solution be free from undissolved particles?

A. Yes.

Q. You are familiar with the Pharmacopoeia of the United States, are you not? [28] A. Yes, sir.

Q. You share the views that are expressed on page 221 of this authority? This is an authority, is it not?

A. I accept it as law.

Q. Referring to what I have marked: "Appearance of Solutions or suspensions," would you read that audibly and then state whether or not you share that view, that two brief paragraphs?

A. "Injections which are solutions of soluble medicaments must be clear, and free of any turbidity or undissolved material which can be detected readily without magnification when the solution is examined against black and white backgrounds with a bright light reflected from a 100-watt Mazda lamp or its equivalent.

(Testimony of Clinton H. Thienes)

"When preparing an injection containing suspended medicament, pass the drug through the standard sieve of at least 200-mesh or employ equivalent treatment in a colloid mill."

Q. Do I understand that is likewise your view?

A. Yes.

Q. Doctor, in your opinion does the solution, as you now see it before you, meet the definition that is contained in the Pharmacopoeia?

A. No; it is my opinion that it does not. [29]

Mr. Neukom: That is all, Mr. Stick.

Cross Examination

By Mr. Stick:

Q. Are you familiar with this product called "Pluri-B" as a general product?

A. I don't know what you mean by that question, sir. I have seen it—I have seen a product either with this name or a similar one in the case of representatives who have come to my office.

Q. And this Pluri-B, being this type of product, is manufactured by more than one concern, more than this defendant, to your knowledge?

A. Similar mixtures are manufactured; yes.

Q. Doctor, is it customary for a doctor to look at a bottle of solution from which he is going to take material for an injection to see whether it is free from suspended particles or undissolved material?

A. It is customary.

Q. And if a doctor were to look at either of those bottles and see that suspended material in it, would the doctor use it? A. No; not the average doctor.

(Testimony of Clinton H. Thienes)

Q. As a matter of fact you would not expect any doctor to use it if he saw particles of that kind in it? [30]

A. Yes; I think perhaps a doctor might.

Q. You think he might?

A. Some doctor might.

Q. How would he give that to the patient if he was giving a dose out of either of those bottles?

A. He would withdraw it with a syringe and needle and—

Q. That is, he would insert the needle into the bottle through the rubber diaphragm which acts as a cork in the top? A. That is right.

Q. And while it was in there, he would then draw out a certain quantity into his syringe? A. Yes, sir.

Q. And then he would withdraw the needle from the bottle and inject it into the patient?

A. That is right.

Q. Would those larger particles in there go through the needle of a syringe?

A. It depends on the size of the needle.

Q. All right. What size of needle is ordinarily used in that type of injection?

A. From an 18 to—from about a 22 to a 16-gauge.

Q. Would they pass through that, either of those?

A. Many of these particles would pass through at 22-gauge needle; yes.

Q. That is many of the smaller particles? [31]

A. Yes.

Q. But the larger ones would not?

A. I think the largest particles would probably not enter even a 16-gauge needle.

(Testimony of Clinton H. Thienes)

Q. Have you ever examined any of the so-called Pluri-B solutions that are on the market? Do you ever use them?

A. I presume by that term you mean B Complex solutions. "Pluri-B" I take it is a trade name applied to this one product, and not to all vitamin B complex products.

Q. All right; a solution similar to that; are you familiar with them and have you used them?

A. Yes.

Q. Did you find any undissolved particles in any of them that you used?

A. I don't recall of seeing any in any that I ever used.

Q. Did you ever examine carefully?

A. Oh, yes.

Q. In this Pharmacopoeia from which you read, you read this portion:—

Mr. Neukom: Page 221.

Q. By Mr. Stick: "When preparing an injection containing suspended medicaments"—
is that the way you pronounce it?

A. That is the right way. [32]

Q. —"pass the product through a standard sieve of at least 200-mesh or employ equivalent treatment in a colloid mill"? A. Yes, sir.

Q. Doesn't that recognize that there will be in suspension certain particles in injectable material?

A. Only in a very restricted number, sir.

Q. But it does recognize that they can be there?

A. It would seem so.

(Testimony of Clinton H. Thienes)

Q. And when they are there, it gives you a recommendation as to what to do to get rid of them; isn't that true?

A. It gives that recommendation to the manufacturers, and not to the doctor.

Q. That is not to the doctor? A. Oh, no.

Q. Do doctors have the Pharmacopoeia?

A. A few of them.

Q. Do you know anything about the precipitation of riboflavin in solution?

A. I know something about it.

Q. And of thiaminehydrochloride? A. Yes.

Q. Could you tell from the precipitate in those bottles whether that precipitate is either thiaminehydrochloride or riboflavin? [33]

A. No; I could not by just looking into the bottle this way. I would have to test it chemically.

Q. Do you know what the precipitate in those bottles is? A. No, sir.

Q. Have you ever seen those bottles prior to August the 1st of 1946? A. No.

Q. When did you first see them?

A. I don't know that I have seen them before this morning. I saw a couple of bottles yesterday, but I don't know that they were these two bottles.

(Testimony of Clinton H. Thienes)

Q. Would a 200-mesh sieve remove the particles that are in that solution if the solution were passed through it?

A. It would remove most of it. I think some of the particles would pass through.

Q. Would those that would pass through be harmful to inject?

A. If injected intravenously, yes; and even intramuscularly, they might.

Mr. Stick: They might. That is all.

Mr. Neukom: I have a couple of questions. [34]

Redirect Examination

By Mr. Neukom:

Q. Doctor, you note in Government's Exhibit No. 2 the size of the labels here, do you not? A. Yes, sir.

Q. If they were glued to the vials would they retard the doctor's ability to detect the particles?

A. It would make it difficult; yes.

Q. Doctor, does a busy practitioner use a solution of the B complex, of which this is, I understand you to say, of such a character, is it not?

A. It is a B complex mixture; yes.

* * * * * * * * *

The Court: Sustained. The answer is stricken.

Q. By Mr. Neukom: Doctor, in your opinion as a physician and surgeon, in purchasing a sterile solution for intravenous and intramuscular use would you expect the

(Testimony of Clinton H. Thienes)

solution to be free and clear from undissolved particles?

A. All except certain special preparations such as bismuth salts, which are used in medicine and are not soluble [35] but are in suspension. They are used with very special care.

Q. I am referring to the B complex?

A. But the B complex should be entirely free from percipitable matter.

Q. And that is the view of a practicing physician who is using such product, isn't it? A. That is true.

* * * * * * * * *

Recross Examination

By Mr. Stick:

Q. Doctor, isn't it a fact that many estrogenic substances have suspended particles in them and are used in injections?

A. You will have to define the meaning of "many" there.

Q. Have particles?

A. Some, but relatively infrequently used. Estrogenic preparations have suspended particles and these are used with very special care and are injected only intramuscularly.

Q. Doctor, isn't it true that any good doctor will [36] always use extra special care? A. Certainly. [37]

* * * * * * * * *

ARNOLD E. MASON,

called as a witness by plaintiff, being first sworn, was examined and testified as follows:

The Clerk: Please state your name.

The Witness: Arnold E. Mason.

Mr. Neukom: We are going to Count I now, your Honor.

Direct Examination

By Mr. Neukom:

Q. Were you at one time employed as a chemist or analyst by the Food and Drug Administration of Washington, D. C.? A. Yes, sir.

Q. And you are not now so employed, are you?

A. No; I am not.

Q. Just what is your employment at the present time?

A. At the present time I am employed as a pharmacologist with Crystal Laboratories, Syracuse, New York.

* * * * * * * * *

Q. In the fall of 1945 you were employed by the Food and Drug Administration as a chemist or pharmacologist? [38] A. Pharmacologist and analyst; yes.

Q. Give briefly your qualifications, your schooling, what you have done.

A. Received a Degree of Bachelor of Science from the University of Nebraska; Master of Science in Physiology from the University of Michigan. I have attended school part time in Washington, D. C., Georgetown University, working on a Degree of Doctor of Philosophy.

Q. You were employed by the Federal Food and Drug Administration as pharmacologist for about how long?

A. For about three years.

(Testimony of Arnold E. Mason)

Q. As a part of your duties, working under your superiors, did you have occasion to analyze various products that were submitted to you? A. Yes, sir.

Q. Did you have occasion in the fall of 1945 to conduct an analysis for the purpose of detecting the existence or lack of posterior pituitary in a product known as "Indoform"?

* * * * * * * * *

A. I ran an essay or tested that product on February 15, 1946.

Q. I will show you a vial here—

May the vial be marked Government's next in order for identification, and a sheet of paper which contains a label [39] be marked to follow for identification?

The Witness: There are code numbers on there.

Mr. Neukom: The numbers, the other writing on here, your Honor, is inspectors' initials and dates and things such as that, which is customary in a case of this kind.

The Clerk: This vial will be Government's 3 for identification and the label will be 4 for identification. The label bears the words "Sterile Indoform."

Q. By Mr. Neukom: Taking the vial, can you note a seal there bearing your initials and date and analysis?

A. Yes, sir. The date of my analysis is scratched into the vial with a diamond pencil.

Q. Right on the glass itself?

A. Right onto the glass.

Q. And what is the date, approximately?

A. The date, I believe, is hidden by one of these seals.

Q. What do your notes show?

* * * * * * * * *

(Testimony of Arnold E. Mason)

A. Among my notes, I have the original inspector's seal here, which indicates that I examined this on February 18, 1946.

Q. And that refreshes your memory as to the date?

A. Yes, sir. [40]

Q. You examined the contents of that vial, Government's Exhibit 3 for identification, for what substance, if any?

A. I examined it to determine whether it had the labelled quantity of posterior pituitary.

Q. First, give what you found, and then we will go over the manner of means used in determining. I note from the label, Government's Exhibit No. 4 for identification, there is an indication that this Sterile Indoform contains posterior pituitary 3 international units per each cc. Incidentally, what is a "cc" in laymen's terms, a cubic centimeter?

A. A cubic centimeter is a small quantity which is used by chemists to measure liquid.

Q. About 20 drops?

A. About 16 to 20 drops in laymen's language.

Q. And 3 international units of posterior pituitary in each cc. Now, Mr. Mason, after you had conducted your tests, which we will go into later, what amount of posterior pituitary did you find, if any, that existed in this product?

A. I found practically no posterior pituitary in that product, an almost immeasurable quantity.

Q. Now, this is a little process that you went into. Are you going to resume this afternoon, or shall I start in on this, your Honor? I was going to make a diagram

(Testimony of Arnold E. Mason)

or map of this. But first, did you use the uterus or some sub- [41] stance from guinea pigs?

A. I used the excised uterus of a virgin guinea pig, which is standard tissue to be used in conducting this test.

Q. And that is the accepted test?

A. That is accepted.

Q. Explain briefly to the court just what you do. Take a virgin guinea pig and kill it, I assume; and then go ahead and explain it.

A. An assay, as given in the United States Pharmacopoeia, states that you must use virgin female guinea pigs of a certain weight. The guinea pig is killed; the uterine horns are removed from the body—

Mr. Neukom: Speak up a little louder.

A. —and suspended in a solution which is somewhat analogous to the solution that that tissue is bathed in in the body, and kept at a temperature corresponding to body temperature of the animal. That tissue, then, when treated with certain substances, will react the same as it would while it is in the body, and by so reacting with a standard solution of known potency—

Q. Let us define our terms. You say "standard solution of known potency"?

A. A standard solution is a solution of posterior pituitary powder. The powder is made into a solution, and by "standard" I mean that the activity of that solution is known [42] to be such that each ½ milligram contains one unit of posterior pituitary activity. The stand-

(Testimony of Arnold E. Mason)

ard powder is the same as the international standard powder, and the solution is made up by the analyst according to the form given in the United States Pharmacopeia. By determining what the excised tissue will do when it is treated with that standard solution, one can determine what any unknown solution will do by comparing the reaction of the unknown solution with the standard.

Q. Were the horns of the uterus of the guinea pig excised and cut and used within a short period of time after the death of the guinea pig?

A. They were removed from the body and within a matter of a very few seconds placed in this solution which the U.S.P. prescribes to be analogous to the fluid surrounding that tissue in the guinea pig.

Q. Do you have a gauge? When you suspend a portion of uterus do you have some device or gauge that displays the contraction or the relaxtant, whatever it is, of the uterus muscle?

A. The uterine muscle is so suspended in a bath at a constant temperature and hooked to two levers such as that a recording can be made of the contraction of the uterus whenever it is caused to contract by posterior pituitary.

Q. Posterior pituitary does cause a contraction, is that right? [43] A. It does cause a contraction.

Q. Of course, the absence of it would be negligible in the spasm of the contraction of the uterus?

A. That is right.

(Testimony of Arnold E. Mason)

Q. Is that uterus in such a condition that it will also still show a little movement even though it was just in plain water? I mean is there some movement upon your machine that you use to gauge it with?

A. The uterus must be kept in the solution prescribed in the U.S.P. to remain alive. If it is not kept in the solution, it cannot be used in this assay. While it is in that solution it will have some automatic contractions.

Q. And did you endeavor to, and is it your opinion, that you adhered to the accepted mode of making this test? A. Yes, sir.

Q. And did you have a cycle made showing the contraction of this particular test?

A. I have made a tracing showing contractions of this particular test.

Q. The tracing machine does something similar to an electric electrocardiograph machine or a barometer reading on a needle, is that right? A. Yes, sir.

Q. Do you happen to have that one here?

A. The tracing of this particular test is the bottom [44] tracing.

Mr. Neukom: May this be marked for identification? Counsel has not seen it.

The Clerk: Marked 5 for identification.

Mr. Neukom: I would like to offer into evidence Government's 3 and 4, so I do not forget to make my offer, unless there is some objection to them.

The Court: Exhibits 3 and 4 for identification are received into evidence. [45]

[GOVERNMENT'S EXHIBIT NO. 4]

30 cc Vial STERILE No. 92

INDOFORM

EACH CC CONTAINS:

Suprarenal Cortex	30 grs.	Whole Ovarian	40 grs.
Anterior Pituitary	30 grs.	Thymus Substance	15 grs.
Posterior Pituitary	3 Int'l Units	Thyroid Substance	1 gr.
		Lymphatic Substance	5 grs.

Preserved with Chlorobutanol (Chloroform Derivative) 0.5% (w/v) and Tricresol 0.5% (v/v)

This preparation does not contain any known therapeutically useful constituent.

CAUTION: To be used only by or on the prescription of a physician.

PASADENA RESEARCH LABORATORIES, Inc.
Pasadena 8, Calif., U. S. A.

Lot No. 728

[Written]: PD-12694 27131-H 728 2-18-46 R. E. Mason 4 for ident.

Case No. 19223. U. S. vs. Pasadena Research Laboratories. U. S. Exhibit 4. Date 6/17/47. No. 4 Identification. Date 6/17/47. No. 4 in Evidence. Clerk, U. S. District Court, Sou. Dist. of Calif. L. J. Somers, Deputy Clerk.

No. 11690. United States Circuit Court of Appeals for the Ninth Circuit. Filed Aug. 25, 1947. Paul P. O'Brien, Clerk.

(Testimony of Arnold E. Mason)

* * * * * * * * *

Direct Examination (Resumed)

By Mr. Neukom:

Q. Mr. Mason, you were testifying with regard to Counts I and II, the product known as "Indoform," a trade name, and with regard to posterior pituitary, the difference or lack of sameness of the product. You had told us about the test which you had performed in conjunction with the uterus of the guinea pig. In conjunction with that test which you performed was there a graph or a sort of a picture made as you were running some of the tests? A. There was.

Q. I show you Government's Exhibit No. 5 for identification and ask you if that is the original graph itself of a portion of the test of the product involved here that you were testing? A. That is.

Q. Now, I have marked and put a little—I don't know [47] what they call them—a little circular white object on one item. Immediately below that, is that a display of one of the tests that you conducted?

A. That is a display of one.

Q. I put this little white arrow, piece of paper I have fastened on there, and does that indicate a portion of the other test? A. It does.

Q. All of the other lines and graphs that are on there, with the exception of the two I have indicated, have nothing to do with this particular product, is that correct?

A. No; that is right.

Q. They were run on the same type sheet?

A. That is right.

(Testimony of Arnold E. Mason)

Q. About the same time, of other products?

A. That is right.

Q. Just explain to the court what you did in running the tests of this product to ascertain whether it has posterior pituitary upon the horns of the uterus as you had it suspended. Did you use some other substance in the comparisons you made; and if the court wants you to, you indicate there on that graph the results?

A. In the first place, the guinea pig uterus is considered an animal tissue which will show quantitatively the amount of pituitary, posterior pituitary, which is given to it. [48] A standard solution of posterior pituitary is made up from a reference standard powder, a United States Pharmacopoeia reference standard powder, which is identical with international posterior pituitary powder.

This reference standard solution is then used to tell to what extent the uterus will contract with a given amount of standard solution. We want to know how much the uterus will contract with a given amount of standard solution. We can then give various doses of any unknown solution containing the posterior pituitary, and by comparing the reaction obtained from the standard solution and the reaction obtained from the unknown sample it is possible to calculate how many units of posterior pituitary are in the unknown preparation.

Q. Or its lack?

A. Or its lack. If there is no reaction or little reaction, it indicates that there is not an amount equivalent to the standard.

(Testimony of Arnold E. Mason)

Q. In this instance how strong was your standard; what was the gauge that you used?

A. A standard solution is made in ampules such that it contains two units of activity per cubic centimeter.

Q. Of posterior pituitary?

A. Of posterior pituitary reference standard.

Q. All right. Now, show to the court this particular item that I have the little white circle over. [49]

I have shown this to counsel prior, your Honor, and counsel wishes to follow.

Will you explain this little item, this graph here, just what was occurring? Was there a needle running on this black sheet of paper, Government's Exhibit 5?

A. Is it possible to use a blackboard?

Q. Yes; if that helps.

(Witness diagrams on blackboard.)

The Court: You are referring to the graph and the words and figures opposite that appear in the lower left corner?

The Witness: Lower right-hand.

The Court: Oh, it is the lower right-hand—

The Witness: Yes.

The Court: —corner of Government's Exhibit 5 for identification?

The Witness: That is right.

This will be a glass jar, chamber of some sort, and to make this drawing accurate, inside of this is another chamber. This is filled up with water which is kept at a certain temperature.

The Court: That is the outer container?

(Testimony of Arnold E. Mason)

The Witness: That is the outer container. The inner container is marked to contain a definite amount of solution which is prescribed by the United States Pharmacopoeia to be used in this assay. The solution, which is a governmental [50] solution for the muscle—the muscle is suspended in this solution and is held at the bottom by means of a hook.

The Court: Now, that is the uterine muscle?

The Witness: The uterine muscle. Another hook is placed in the top of the uterus muscle and a string is attached, going up and out of this bath, we might call it, and attached to a lever. This lever will be placed here. When pituitary solutions are added to the bath, this inner bath, it causes the muscle to contract or shorten. As the muscle shortens it pulls on this lever and the lever will go up. This lever has a pointer on it and is touching a drum, and that drum is a piece of paper which has been smoked by means of bubbling benzine through natural gas. Therefore, every time this lever goes up and down again it makes a scratch mark on the paper.

The Court: The recording needle is at the one end of the lever, is that right?

The Witness: That is right; recording the action of this muscle. Then when this paper is filled up or we are done with that particular work, the paper is removed and run through shellac for permanent record.

Q. By Mr. Neukom: And that is Government's Exhibit 5 for identification?

A. That is Government's Exhibit 5 for identification. In that right-hand corner of this exhibit, this is what has [51] happened.

(Testimony of Arnold E. Mason)

Q. Explain the time element as you do this, too, please.

A. All right. The muscle is attached here. It takes sometime for it to relax and to become normal after removing it from the body.

We will assume that this drum is moving constantly very slowly. If the drum is moving and this pointer is at this point on the drum, it will get a line. However, it is not usually a straight line because there is some constant automatic contracting of this muscle, including the uterine muscle. We may go along like this and get very little jog in that line. At this point in the record, to use the record for an example, at this immediate point the record is labeled: 1-B, one-half or five-tenths cubic centimeter, S_1. "S_1" indicates on this record the first solution of standard reference posterior pituitary that I had used in this test.

Then it says: 1-50 there. The standard preparation, as I mentioned a while ago, contains two U.S.P. units per cubic centimeter.

The guinea pig uterus is so sensitive to posterior pituitary activity that it is necessary to dilute that. This standard has been diluted 50 times. In other words, 1 cc of standard solution is diluted to 50 ccs with physiological salt solution. [52]

That has a time on the record, "12:42". Then there is another figure there, "13.5".

At this point a half a cc of standard preparation, diluted 50 times, is added to the bath. The muscle contracts; it contracts and, from experience, it is possible to tell when it is done contracting. As it is done contracting, the lever is lifted off of the drum, because as

(Testimony of Arnold E. Mason)

soon as it is done contracting it is removed. The internal muscle bath—

The Court: You mean the inner chamber—

A. The inner chamber.

The Court: —containing the muscle?

The Witness: That is right; has a tube, so that everything can be sucked out of that inner chamber. The muscle is washed with the normal bath so that it is not affected by any posterior pituitary solution.

The Court: By that do you mean that when you reach the point where the muscle contracts once, and at the time you estimate that that process, that first contraction, has reached its limits, you lift the needle, then drain the inner container, wash the muscle and start all over again; is that it?

The Witness: That is right.

The Court: And repeat the same process?

The Witness: The only reason the needle is lifted is because, if it is not lifted, when this chamber is drained and refilled the needle will go all over and make a rather [53] smudgy record.

Then as the chamber is refilled with fresh solution containing no pituitary activity, the muscle relaxes in a fashion similar to that and shows some more of these automatic contractions.

The Court: In other words, you have a down graph?

The Witness: That is right.

The Court: From the contraction you have, indicates that is a down graph?

The Witness: That is right.

This "13.5" represents millimeters that the muscle has contracted on the graph.

(Testimony of Arnold E. Mason)

Then this muscle has relaxed at this point and is ready again to show activity when pituitary solution is given to it. That is a period of 12 minutes there.

The next thing that appears on the record—

The Court: Is that always so, 12 minutes?

The Witness: 10 to 15 minutes. In 90 per cent of the tissues used, uterus muscles used, it will be 12 minutes.

The next thing on this record is labeled "2-B". "2-B" merely indicates a—

The Court: A repetition of the same experiment?

The Witness: Indicates the next step in this experiment. This is the first step. "2" represents the second step in this particular record. The "B" indicates the record on the [54] lower half, the tracings on the lower-half of this record.

"A" is the top half.

Here this muscle was given a half a cc of 12694, which is a number which has been assigned to a sample in the Division of Pharmacology, Food and Drug Administration, by that division, and that number corresponds with a Government number of the sample which has been assigned to it by an inspector.

The Court: Let me see if I am clear. "1-B" represents the test with the standard solution?

The Witness: That is right.

The Court: Now, "2-B" is to represent the test with the solution that is under investigation?

The Witness: That is right. This number is for my own identification of that particular sample.

Then I have "fs." here, and there is another record of time here, "12:54", which indicates that that was

(Testimony of Arnold E. Mason)

12 minutes after the standard solution was given. There is no record of any contraction.

This is about what the record looks like, I believe. That was left in there, the sample, half a cc, and this sample was left in the bath surrounding the uterine muscle for a time equivalent to the time it was in under when the standard solution was given.

Q. By Mr. Neukom: Under "1-B"?

A. Under "1-B". No reaction occurred. So, again, the [55] muscle bath was washed, the muscle was washed, in other words, and the muscle showed this relaxation again.

At "3-B" the same test of standard pituitary solution was given as at 1-B.

Mr. Neukom: Writing down figures on the blackboard.

The Court: In other words, you repeated the test with the standard solution?

The Witness: Repeated it.

The Court: To ascertain if the muscle would still react to that solution?

The Witness: To be certain that the muscle was not dead, so to speak. Something like this happened: The muscle showed it was going to relax, and again it was washed out and returned to normal. Now—

The Court: What relaxation did it show? What contraction did the muscle show the second time you subjected it to the standard solution?

The Witness: It contracted a little more than it did the first time, 16½ millimeters, whereas in the first case it contracted 13½, the difference of 3 millimeters. The reason for that is probably that it has actually had a

(Testimony of Arnold E. Mason)

long rest here, longer than 12 minutes, since there was little or no activity shown up to this point.

The Court: By "long rest" you mean a long rest between the first application of standard solution and the second [56] application of standard solution?

The Witness: That is right. The standard solution "S," is made from a preparation containing two units per cubic centimeter. The 12694—

The Court: That is the solution under investigation?

The Witness: Under investigation, was labeled to contain 3 units per cubic centimeter. The standard solution, in order to be used, had to be diluted 50 times. This one had to be diluted 50 times because the muscle was that sensitive to pituitary.

The Court: Just a moment. Let me understand that. You mean in order to make a test you had to dilute it?

The Witness: In order to make a test.

The Court: You diluted it down to—

The Witness: This would have been—

The Court: —what percentage of units per centimeter?

The Witness: This would have been diluted down to point—this reference, ".04".

The Court: Cubic centimeter?

The Witness: Units per cubic centimeter. It would be 1-50 cc to .04 units.

The Court: Four one-hundredths of a unit, is that it?

The Witness: Yes; four one-hundredths of a unit. The solution under investigation should have been diluted a corresponding amount and should have given a contraction at a [57] corresponding height in order to contain the labeled amount of three units per cubic centimeter.

(Testimony of Arnold E. Mason)

However, in this test, as you can see, it was not diluted at all; it was used full strength and it still does not give a reaction. In other words, it was over 50 times as strong as the standard and still did not give a reaction. It was impossible to give enough of it to cause the contraction equivalent to the standard.

The Court: The solution under investigation is labeled to contain 50 per cent more in strength per cubic centimeter?

The Witness: That is right; or three units per cubic centimeter, and was not diluted at all, whereas the standard was diluted 50 times.

Q. By Mr. Neukom: Mr. Mason, you conducted this examination on what date? What was the date there?

A. February 18, 1940.

Q. Let us assume that this product was shipped on September 17, 1945, which is a matter of around five months, is it not, or thereabouts?

A. That is right.

Q. Is posterior pituitary a stable product?

A. It is very stable except at excessively high temperatures.

Q. Except at what?

A. Except at excessively high temperatures. [58]

The Court: What do you mean by "excessively high temperatures"?

The Witness: A temperature of boiling of a fairly long time, say, a few hours.

The Court: Translate that into degrees.

The Witness: 212 degrees Fahrenheit or 100 degrees Centigrade.

The Court: Or better?

(Testimony of Arnold E. Mason)

The Witness: Or better, for, say, five or six hours, then it will break down.

Q. By Mr. Neukom: In normally warm temperatures, even up to 120, like may occur in the desert, that would not affect it, would it?

A. It would not affect it.

Q. When I asked you if it is stable, does that also mean that it continues its effectiveness for many months and even years? A. Yes, sir.

Q. Now, with that in mind, have you an opinion as to whether or not the product that you examined, known here as "Indoform", whether or not it contained posterior pituitary in three international units?

A. It did not.

Q. Did it contain any posterior pituitary or, if any, approximately in what amount? [59]

A. I would say an amount which is not measurable, if any.

Q. Did it, in your opinion, contain any posterior pituitary at the time it was shipped on September 17, 1945?

Mr. Stick: I object to that as a matter that cannot be testified to by this gentleman, unless all of the conditions and factors under which this matter was kept, handled and existed between the time when it was shipped by the defendant to the time when he first saw it is also before him.

The Court: That is the ultimate fact to determine, is it not?

Mr. Neukom: Yes, your Honor.

The Court: Objection sustained.

Mr. Neukom: May I be heard? If that was the rule, your Honor, then he could not express an opinion as to

(Testimony of Arnold E. Mason)

whether or not the product that he examined did or did not contain a certain amount as of such and such a date, and we would not have any Food and Drug cases.

The Court: He can cover and has covered it.

Mr. Neukom: Well, except he has not expressed a fact opinion, your Honor.

The Court: But it seems to me it goes one degree beyond what an expert or any witness should be permitted or competent to say, and that is: Did the defendant commit the offense.

Mr. Neukom: Well, I do not exactly agree with you. It [60] would be so if we were going to evade a factual matter which was not susceptible of expert opinion.

Now, if we pick up a piece of gold today and a man says that it is so many carats of gold, if he is a metallurgist or knows something about it, why, he would be privileged to say that a year back it was 18 carat, too.

The Court: Yes; I take it that he might say in response to a hypothetical question, assuming that it was not subjected to excessively high temperatures which you have described, assuming it was not diluted, assuming that it was in the same physical condition as it was when you examined it, in your opinion, was—

Mr. Neukom: Then I will reframe it in this manner. I had thought that I had covered it by my other questions and, therefore, had not propounded the assumption question.

Q. Assuming, Mr. Mason, that this product was not exposed to excessive temperatures, that is to say, that you said was 212 degrees is the destructive temperature; and assuming the product was handled in a normal and careful manner, retained in the bottle, as Government's

(Testimony of Arnold E. Mason)

Exhibit No. 4, I believe; assuming which bottle you opened and conducted the test as you have testified; and, with the assumption of what you found or did not find at that time, have you an opinion as to whether or not this product contained three international units of posterior pituitary on September 17, 1945? [61]

Mr. Stick: The same objection.

The Court: Overruled.

A. It is my opinion that the product could not have contained three units of posterior pituitary per cubic centimeter on September 17, 1945.

Q. By Mr. Neukom: Now assuming that all that you have testified to here and the explanations you have given, what is your opinion, carrying on the assumptions that I have enumerated—what is your opinion as to the amount, if any, of posterior pituitary was in the product on or about September 17, 1945?

A. On that date, September 17, 1945, it is my opinion that there was a quantity of posterior pituitary present which was not measurable by the standard methods of measuring it or there was none.

Mr. Stick: Pardon me. That is under the same conditions as in your first question?

Mr. Neukom: Yes; assuming.

A. Assuming that it is kept under normal conditions.

Q. I might ask, further, is posterior pituitary required to be kept in an ice box?

A. I do not remember that statement on the label of this sample.

Q. Well, assuming that this—well, that is a matter for the court. When you looked at the label on this

(Testimony of Arnold E. Mason)

particular sample 4, did you note any caution or comment as to the mode of [62] keeping this product?

A. There is no statement regarding the storage of this product.

The Court: That is exhibit?

Mr. Neukom: 4, your Honor, in evidence.

Q. But, in your opinion—I am asking you your opinion as to whether or not posterior pituitary—you have stated that it breaks down at about 212 degrees, is that correct? A. That is right; it may.

Q. Well, under that, does it have a tendency to break down and lose its efficacy? A. It does not.

Q. Did you add anything to this product or substitute anything to the bottle in conducting your tests?

A. No; I did not.

Q. And after you had concluded your tests of this bottle, Government's Exhibit 3, what did you do with the bottle then?

A. After conducting the test, the bottle was replaced in a locked refrigerator until the next day; then I wrapped it and put a seal on it and it was sent to San Francisco.

Q. You caused it to be sent as a part of your official duties, is that correct? A. Yes, sir.

Q. To the analysts in San Francisco? [63]

A. Yes, sir.

Q. And this Government's Exhibit No. 3, does it have one of the seals on there with your initials?

A. This has the seal on it that I originally put on the package that the bottle was in.

Q. Your initials appear on there?

A. My name; yes, sir.

(Testimony of Arnold E. Mason)

Mr. Neukom: Under your name. I would like to offer into evidence Government's Exhibit No. 5 for identification, but with the understanding that the other graph marks, other than as indicated, have no bearing on the case. Those constitute part of another test.

The Court: Exhibit 5 for identification received into evidence.

Mr. Neukom: That is all.

The Court: At the time you first received this bottle, Exhibit 3, how was the top of it sealed, if it was sealed? Did it contain a cork?

The Witness: As I recollect, it contained a rubber stopper. I cannot be certain without again looking at the bottle. The same stopper would still be on it.

The Court: Mr. Clerk, will you hand the exhibit to the witness, please?

The Witness: It contains a rubber stopper, your Honor.

The Court: Is that a rubber stopper similar to a cork, [64] what we call commonly a cork?

The Witness: Yes. Part of the rubber stopper serves as a cork and goes down inside the neck of the bottle.

The Court: Was that cork sealed into the bottle in any way?

The Witness: I do not remember whether it was sealed into the bottle or not. It has the same type of rubber stopper that is commonly on such preparations.

* * * * * * * * *

The Court: Mr. Clerk, will you exhibit or show the witness the containers in Exhibit 1, the two bottles in Exhibit 1?

(The clerk exhibits said bottles to the witness.)

(Testimony of Arnold E. Mason)

The Court: Was the bottle, Exhibit 3, at the time you received it corked or closed and sealed in the same manner or a similar manner?

The Witness: It was sealed in the same manner as Exhibit No. 1.

The Court: As those bottles, those two bottles?

The Witness: As those two bottles.

The Court: That is all I have.

Cross Examination

By Mr. Stick:

Q. Mr. Mason, this seal that you speak about on these [65] bottles and call a cork is actually a material which clamps around the outside and has a small rubber diaphragm, thin diaphragm, in the center; isn't that true?

A. The rubber cork goes down into the neck of the bottle for a short distance, folds around the outside of the bottle, then is sealed with a plastic seal.

Q. And the center of the cork is a very thin membrane of rubber; isn't that true?

A. That may only be determined in that particular cork by cutting the cork up.

Q. Isn't it true that they have that so the hypodermic needle can be run through the center diaphragm and the solution taken out? A. Yes; that is usual.

Q. Isn't it true that that is the standard and usual practice?

A. That is the standard practice of using a needle.

The Court: Did this Exhibit 3, when you received it, the bottle, appear to be so corked?

The Witness: Yes, sir.

The Court: As counsel has just described it?

(Testimony of Arnold E. Mason)

The Witness: Yes, sir.

The Court: That is, corked and sealed?

The Witness: Corked and sealed.

Q. By Mr. Stick: Generally, the type of cork would be such as the type of cork that is on the bottle I now hand [66] you to look at?

Mr. Neukom: May that be identified as, maybe, defendants' A, your Honor?

The Court: Yes; it may be marked for identification as Defendants' Exhibit A. A. Yes, sir.

Q. By Mr. Stick: And there is in the top of that a small depression which is the part where the needle is usually inserted for the purpose of withdrawing a part of the contents; is that not true?

A. That is true.

The Court: Now, did this bottle, Exhibit 3, at the time you first saw it appear to be corked and sealed in the same manner as Defendants' A for identification?

The Witness: In the same or a similar manner.

Q. By Mr. Stick: Did you make any examination of the cork that was on the bottle which you investigated as to its condition, or whether it had been used or whether it had been punctured by a needle? Did you make any independent investigation of that point?

A. No; I did not examine the cork in that fashion.

Q. Now, Mr. Mason, in making this test that you have made and explained here, you used the tests or followed the test that is laid down in the Pharmacopoeia of the United States of America? [67]

A. I followed that procedure.

(Testimony of Arnold E. Mason)

Q. Now, what is the accuracy of that test?

A. The accuracy of that test, as is given in the United States Pharmacopoeia, is plus or minus 20 per cent.

Q. Plus or minus 20 per cent?

The Court: By that, do you mean that you should allow to that extent, 20 per cent for error?

The Witness: That is correct.

The Court: You tested and found a certain number of units, according to your test, and you should allow 20 per cent more, is that it?

The Witness: If I had tested a preparation and calculated it on a percentage basis, and it came out 82 per cent of labeled potency, I would assume that the 18 per cent—that it could have been 100 per cent, and that the 18 per cent difference might be due to errors in the assay, which are possible, and to the variation in the animal tissue.

Q. By Mr. Stick: Would you state again just how you prepared this standard solution that you made?

A. A reference standard posterior pituitary powder is received from the U. S. Pharmacopoeial committee on revision in a sealed ampule. Upon immediately receiving that powder it is dated, initialed, and placed in an ice box. Whenever a standard solution to be used in assay is to be prepared, the powder is removed from the ice box, the ampule broken, and the [68] powder carefully weighed and made into a solution according to the directions in the United States Pharmacopoeia.

That solution is then sterilized and put into hard glass ampules, the ampules sealed, labeled, and placed again in a locked ice box. The solution is made up to contain two U.S.P. units per cubic centimeter. Then the solution

(Testimony of Arnold E. Mason)

in this case is made up by two individuals to insure accuracy.

Q. How do you mean made up by two individuals?

A. There were two individuals present while the standard solutions were being made up.

Q. Who made them up?

A. Dr. Vos, in Washington, D. C., and myself.

Q. Were you both present at the time?

A. We were both present.

Q. Why do you place these solutions, this powder, in an ice box?

A. Why did I place it in the ice box?

Q. Yes.

A. The powder is placed in the ice box because that is the one place we have a key. The ice box is locked. All standard preparations are kept in that place under lock so they cannot be tampered with by anyone except the person using them.

Q. What is the temperature of that ice box?

A. I couldn't say exactly. It is an ordinary refriger- [69] ator.

Q. This standard solution that you made, then contained only water and this posterior pituitary powder?

A. The standard solution also contains a very slight amount of acid.

Q. What kind of acid?

A. It contains—it is made up with the standard powder and 25 one-hundredths per cent of acetate acid.

Q. Is that according to the test here in the Pharmacopoeia?

A. That is according to the United States Pharmacopoeia directions.

(Testimony of Arnold E. Mason)

Q. Then, water, pituitary powder and the acetate are all that there was in your standard solution?

A. That is correct.

Mr. Stick: That is all.

Redirect Examination

By Mr. Neukom:

Q. You testified that you sealed the Government's Exhibit No. 3 and then caused it to be sent on to San Francisco; was that your testimony? A. Yes, sir.

Q. And you placed a seal on it, but now you see underneath another seal, is that correct? [70]

A. Yes; I do.

Q. Of course, you don't know how that got there only by surmise, is that correct? A. That is right.

Q. Just one question about the needle here. To what extent, in your opinion, would the needle have been caused to raise from the contraction had this product designated here as "2-B", the product here involved, had it contained three international units and you had made the test of full strength—which you did make it of full strength, I understand, is that right?

A. Yes, sir. The contraction would have gone as high as the muscle was able to contract; that is, the lever would have gone as high as the muscle could have made it go; the maximum contraction which was possible for that muscle would have occurred.

Q. Assuming that the contraction on the standard here was about five inches, in point of inches, and assum-

(Testimony of Arnold E. Mason)

ing on your diagram, have you an opinion as to how far it would have gone?

A. It certainly would have gone over five; it would have gone any place from 10 to 25 inches.

Q. Your needle reading? A. Yes, sir.

Mr. Neukom: That is all. [71]

* * * * * * * * *

The Court: That is all, Mr. Mason.

Mr. Neukom: Mr. Buell.

ANDREW G. BUELL,

called as a witness by plaintiff, being first sworn, was examined and testified as follows:

The Clerk: What is your name, sir?

The Witness: Andrew G. Buell, B-u-e-l-l.

Direct Examination

By Mr. Neukom:

Q. What is your business or occupation?

A. I am a chemist for the United States Food and Drug Administration, stationed at San Francisco.

Q. Were you such in February of last year?

A. Yes, sir.

Q. You have been practicing your profession for about how long? A. About 21 years.

Q. You are a graduate of what school? [72]

A. University of Nebraska.

Q. Specialized in Chemistry there?

A. Yes, sir.

Q. And since then what?

A. I was employed by the United States Patent Office for a year and half, and since then continuously in the United States Food and Drug Administration.

(Testimony of Andrew G. Buell)

Q. You have had occasion, from day to day and week to week all this time, to conduct analyses and examine products for the Government, is that correct?

A. Yes, sir.

Q. In the course of your duties did you receive, being transmitted to you from Mr. Mason, what now has been marked as Government's Exhibit 3 in evidence? And I would like to have you look at the seal on that bottle, the lower seal.

A. Yes, sir; that is my seal there.

Q. And first, so we can take this seal off and see what this cork is like, just tell us this: You did conduct an investigation or an examination of that product after you received it, is that coorrect? A. Yes; I did sir.

Q. And when that produce came to you did it have a seal on it?

A. Yes; it had this top seal of Analyst Mason.

Q. That was glued on there in similar fashion—am I [73] correct—as the seal which is now adhered to and glued to the bottle, is that right?

A. No; that seal—the bottle was wrapped in paper.

Q. Oh, yes.

A. And the paper was sealed.

Q. So that before you could get to the bottle you had to break the seal that I have this rubber band around, the top of the neck of this bottle, is that correct?

A. Yes; I had to break Analyst Mason's seal to get at the bottle.

Q. And you did open that package yourself, is that correct? A. Yes, sir.

Q. And what is about the date that you did do that?

A. On March 27, 1946.

(Testimony of Andrew G. Buell)

Q. Then, shortly after that, after you had conducted your investigation, which I am going to go into here in a moment, did you then reseal the remainder of the contents of this bottle?

A. Yes. After I made my examination, I immediately put my seal on the bottle.

Q. And that is the seal which now seals the bottle?

A. Yes; and dated March 28, the day after I examined it.

Mr. Neukom: Has counsel any objections to my removing [74] the little top part of this seal so that we can see what type of rubber stopper there is?

Mr. Stick: None whatever.

Mr. Neukom: The record may show that I have opened and bent back the seal placed on by Mr. Buell.

The Court: On Exhibit 3?

Mr. Neukom: On Exhibit 3, your Honor. And I will put a rubber band around Mr. Mason's seal, which is a part of the same exhibit.

Q. When you received the bottle did it have that character of stopper that you see there?

A. Yes; it is in the identical condition that it was when I received it.

Q. And before you took any out of the bottle—or, how did you take it out? Did you have a syringe and pull it out in that manner?

A. No. I just removed the stopper and took my portion for an analysis with a pipette.

Q. With a what? A. With a pipette.

(Testimony of Andrew G. Buell)

Q. Did you conduct an analysis upon this product after you had received it to ascertain what, if any, thyroid substance it had?

A. Yes; I examined it for thyroid content.

Q. And after you had given it the test, which you will [75] later relate, what, if any, thyroid did you find this substance had, this Indoform had?

A. There was no thyroid present whatsoever.

Q. Now, will you relate to the court the means that you used to endeavor to ascertain whether or not there was any thyroid in the substance?

A. Well, I made a quantitative determination of organically combined iodine.

* * * * * * * * *

Q. By Mr. Neukom: Incidentally, is there any correlation between iodine and thyroid?

A. The activity of thyroid depends on the organically combined iodine present in the thyroid.

Q. All right. Now, will you tell the court just what you did?

A. Well, I withdrew 15 cubic centimeters of the product.

Q. From Government's Exhibit 3 here?

A. From Government's Exhibit 3, and determined the iodine by the Elmslee-Caldwell method. [76]

* * * * * * * * *

Q. By Mr. Neukom: And what is that method?

A. Well, that is the most acceptable method for the determination of iodine.

(Testimony of Andrew G. Buell)

Q. Now, you keep saying "iodine"; so let us have the explanation between why you were looking for iodine when here we are looking for thyroid.

A. The activity of thyroid depends on the organically combined iodine present. The iodine in thyroid is present as the di-iodo-tyrosine, and also as thyroxine.

The Court: What is that first word you used?

The Witness: Di-iodo-tyrosine.

The Court: In other words, a thyroid tablet or a thyroid medicine contains iodine, is that it?

The Witness: That is right; organically combined iodine. Yes, sir, your Honor.

The Court: What else would it contain?

The Witness: Well, to produce the thyroid, the thyroid glands of sheep and hogs taken and the connective fat tissue is cut off.

Mr. Neukom: Speak up now so Mr. Stick can hear you.

A. The connective fat tissue is separated from the glands, and then it is extracted with petroleum ether to get rid of all fatty matter, and then it is dessicated at about 60 to 60 degrees Centigrade, and then it is later powdered up in [77] this thyroid powder of commerce.

The Court: But the ingredient we get is iodine, is it?

The Witness: Is the iodine.

The Court: The rest of it is just a carrier for the iodine, is that it?

The Witness: That is right, sir.

Q. By Mr. Neukom: You conducted tests that you understand, the approved tests, for endeavoring to determine whether there was any thyroid substance present, did you? A. Yes, sir.

(Testimony of Andrew G. Buell)

Q. I observe on the label here that it says "Tyroid Substance 1 grain" or "1 gr." Is that "grain"?

A. That is one grain; yes, sir.

* * * * * * * * *

Q. Would you look at 4 so we can have an interpretation of what that one grain means according to the label?

A. The label states that "each cc contains Thyroid Substance 1 grain."

The Court: Does that mean contains one grain of iodine?

The Witness: One grain of the active constituent of [78] the thyroid.

The Court: That is iodine?

The Witness: As organically combined iodine.

Q. By Mr. Neukom: In your opinion, or what did your test reveal, in your opinion, as the amount of thyroid substance in this product, Government's Exhibit 3, when you analyzed it in March of 1946?

A. There was no thyroid present at all.

Q. Is thyroid substance a stable product?

A. Yes; it is, sir.

Q. Is it susceptible to early deterioration?

A. It is considered a quite stable product. Even though it was decomposed, I would still have found iodine in the solution because there was no way for the iodine to escape.

Q. Does extreme heat affect the iodine?

The Court: By that, do you mean does it dissipate it?

(Testimony of Andrew G. Buell)

Mr. Neukom: Yes; dissipate it?

A. No; it could not possibly dissipate it, because the bottle was a sealed bottle, and even though it was decomposed, that iodine would have still been in the bottle.

Q. Even had it all evaporated, would there still have been a crystal form remaining?

A. Yes, sir; it would have still been in there.

Q. In your opinion, would the retention of the product [79] in temperature of an ordinary refrigerator, would that dissipate the thyroid substance?

A. No, sir.

Q. Would the normal temperatures rising even up to 120 or more, would that dissipate it? A. No, sir.

Q. Assuming this product had been handled—we will assume taking in conjunction—although I know this question is not entirely proper. You heard the testimony of Mr. Mason, did you not? A. I did, sir.

Q. And assuming that this product here, nothing was added to it, nothing taken from it excepting the amount that chemist Mason took from it; assuming that it was transmitted to you by mail, and the assumption of the findings that you gathered from your tests, have you an opinion as to whether or not this product contained in Government's No. 3 contained any thyroid substance on September 17, 1945?

A. It could possibly have contained no thyroid when it was manufactured.

Q. Assuming the product that you looked at, your opinion back is that it contained no thyroid substance?

A. Yes, sir.

The Court: Would iodine evaporate in any way?

(Testimony of Andrew G. Buell)

The Witness: No. It is organically combined, so that [80] even though the water was evaporated off, the thyroxine and the di-iodo-tyrosine would still be present.

The Court: Suppose you took the contents of this Exhibit 3, and assuming it contained one grain of thyroid substance per each cubic centimeter, and suppose you boiled it, would the iodine or the thyroid substance be dissipated?

The Witness: No; it would still be left. It would still be left and not evaporated off. The water—

The Court: If you boiled it dry?

The Witness: If you would boil it dry, it would still be there.

* * * * * * * * *

Cross Examination

By Mr. Stick:

Q. Mr. Buell, I believe you stated that you used an Elmslee-Caldwell method of test? A. Yes, sir.

Q. For the iodine? [81] A. Yes, sir.

Q. What is that test? How do you perform it?

A. Well, I took the 15 cubic centimeters of solution and put it in a nickel crucible and added 10 cc of alcohol, five grams of sodium carbonate, and five cc of 40 per cent sodium hydrochloric acid, evaporated that down to dryness and put it into a muffle furnace.

Mr. Stick: Into a what?

A. Into a muffle furnace at 550 degrees for one-half hour. And then the extract is—then it is taken out of the muffle, cooled down, and boiling water added to it and filtered, and the melt is extracted until all the iodine present is gone through the filter paper into the

(Testimony of Andrew G. Buell)

flask below. That is made up to 300 cubic centimeters and then phosphoric acid is added to it and bromine is then added, and the iodine, any iodine present, is oxidized to the iodate stage, then the excess bromine that is added is entirely boiled off and the product cooled down and potassium iodide is added and titrated off with sodium sulphate standard solution, and from the number of cubic centimeters of thiosulphate solution the amount of iodine is calculated. That is the sum and substance of the test.

Q. By Mr. Stick: Thyroid is a gland in the body of a living animal, is it not? A. Yes, sir. [82]

Q. And this gland contains certain compounds, does it not? A. Yes, sir.

Q. One of those compounds or substances is iodine, or is an iodine compound?

A. It is organically combined iodine; yes, sir.

Q. Combined with what?

A. Well, it is combined as the di-iodo-tyrosine and also as thyroxine.

Q. Now, thyroxine is then one of the substances in the thyroid gland? A. That is right.

Q. Now, what other substances besides iodine or thyroxine are in the thyroid glands?

A. There is no therapeutically active ingredients other than the iodine-thyroxine compounds.

* * * * * * * * *

Mr. Stick: I am not asking for "therapeutically active" or anything else. What other substances are there?

(Testimony of Andrew G. Buell)

A. Well, muscle tissue would be one of them, probably a little fat that would be undissolved by the petroleum ether in the preparation of the glands. [83]

Q. Would there be any salts of any kind present?

A. Yes; there would be some sodium chloride present.

Q. Anything else?

A. That is about all I would know.

Q. Would there be any proteins?

A. Yes; there would be proteins present.

Q. Fats? A. Probably a small amount of fats.

Q. Would there be any adrenalin present?

A. I don't know.

Q. You don't know. There would be in a thyroid gland, then, things other than iodine or thyroxine or this other substance that you mentioned similar to it, would there not?

A. There would be other things present,

* * * * * * * * *

Q. In your handling of the substance which you took [84] from the bottle, which I believe is Exhibit 3, did you examine what base the contents of that bottle were dissolved in or were held in?

A. No; I did not.

Q. Was it an oil base?

A. I don't think it was oil. It looks like a water solution.

Q. Well, a water base. Is iodine soluble in water?

A. Iodine is, but the organically combined iodine and thyroid is insoluble in water.

Q. Thyroxine is insoluble?

A. Is insoluble in water.

(Testimony of Andrew G. Buell)

Q. What was the name of the other?

A. Di-iodo-tyrosine is the other iodine compound.

Q. And is that soluble in water?

A. That is insoluble.

Q. Then, if this was a water base, you would not expect to find any of those parts of the thyroid gland in the substance?

A. There would be none; no, sir.

Q. There would be none. There could, however, be other parts of the thyroid gland solution?

A. That is possible.

Q. Did you examine the label that was on the bottle, Exhibit 3? [85]

A. Well, when I received the sample the label had been removed for the records. I have since seen the label, though.

Q. Did you see the label at the time that you made your examination?

A. Yes. I received the records and the label was included in the records.

Q. In the records? A. Yes, sir.

Q. I have here Exhibit No. 4, which is a sheet of paper on which there appears a label. Is that the label that you saw at the time that you made this examination and test? A. Yes; it is.

Q. Did you read that label?

A. Yes. That is one of our duties, is to read the label before we start the analysis.

Q. Did you read on there this portion: "This preparation does not contain any known therapeutically useful constituent."? A. I read that, sir.

(Testimony of Andrew G. Buell)

Q. Did that indicate to you that there was no active substance of thyroid in that solution?

A. Well, you would draw that conclusion from reading that; but I did not let that influence me at all when I made my analysis. [86]

Q. So you examined for iodine? A. Yes, sir.

Q. And only for iodine? A. That is right.

Q. And for no other thyroid substance than iodine?

A. That is right.

Mr. Stick: That is all.

Redirect Examination

By Mr. Neukom:

Q. Mr. Buell, did you find anything in this product which you can identify as a thyroid substance?

Mr. Stick: He just said he made no examination in regard to it.

A. The only thing I examined it for was for the therapeutically active ingredients of thyroid, which were the organically combined iodine products.

Q. What do you mean by the "therapeutically active"?

A. Well, the therapeutically active constituent of thyroid is thyroxine and the di-iodo-tyrosine.

Q. Those you did not find?

A. And they weren't present.

The Court: They were not present?

The Witness: They were not present, your Honor.

Q. By Mr. Neukom: Do you know of any other test, [87] either as denominated in the Pharmacopoeia

(Testimony of Andrew G. Buell)

or from your own experience or knowledge, of detecting a thyroid substance other than the one you have related?

A. No; that is the only test that we use, is the one used in the Pharmacopoeia, which is almost identical with the method I used.

Q. Is that the accepted test among chemists and analysts of good repute?

A. Yes; that is a test that all chemists used for a detection of thyroid, is the organically combined iodine method.

Mr. Neukom: That is all. Did you want some questions?

The Court: No; I have nothing further.

Mr. Neukom: Mr. Capps. We have but two more witnesses, your Honor, on the case in chief.

HUBERT H. CAPPS,

called as a witness by plaintiff, being first sworn, was examined and testified as follows:

The Clerk: Please state your name.

The Witness: Hubert M. Capps.

Mr. Neukom: We are now taking up Counts III and IV, your Honor, what is known as the Pluri-B. [88]

Direct Examination

By Mr. Neukom:

Q. Did you have occasion to analyze a substance known as Pluri-B? A. Yes.

Q. And about what date did you conduct your analysis?

* * * * * * * * *

(Testimony of Hubert H. Capps)

The Witness: It was in September, 1945, the 24th, I believe.

* * * * * * * * *

Q. What is your business or occupation, that is to say, as of the date that you just testified to, September, 1945?

A. I was a chemist for the Food and Drug Administration.

Q. And working in Washington, D. C.?

A. That is right.

Q. And assigned to what division?

A. The Vitamin Division.

Q. And had been so employed for about how long prior to that?

A. About six years in the Vitamin Division.

Q. What was your education or background along your [89] specialty line?

A. I have an A.B. from Hardin-Simmons University in Texas.

Mr. Neukom: Speak up so we can all hear you.

A. And I have a master's degree from the University of Washington in Seattle; and I did some graduate work in Iowa State College.

Q. In the chemistry field?

A. Yes; all of it was in chemistry.

Q. And did you have any other experience along that line after graduating, other than that that which you had with the Food and Drug Administration?

A. Well, I taught chemistry up until the time I came with the Food and Drug Administration.

* * * * * * * * *

(Testimony of Hubert H. Capps)

Q. By Mr. Neukom: And while you were with the Food and Drug Administration did you have occasion to analyze various products? A. Many of them.

Q. And particularly in conjunction with ascertaining whether or not products had the substances we commonly refer to as B-1 and B-2? [90]

A. Well, B-1 and C, chiefly; B-1 and Vitamin C.

Q. I see. Incidentally, what is the correct chemical or chemical term for the B vitamin?

A. B-1 is ordinarily called "thiamine" or "thiamine hydrochloride".

Q. And what is "riboflavin"?

A. That is ordinarily called Vitamin B-2. Both of them as B-complex.

Mr. Neukom: Now, I am going to have marked for identification a vial as Government's next in order.

The Clerk: 6 for identification.

Mr. Neukom: And a label on a sheet of paper.

The Clerk: 7 for identification.

Q. By Mr. Neukom: In the course of your duties with the Food and Drug as a chemist, did you have occasion to receive a vial containing a product such as reflected by Government's Exhibit 6 for identification? Did you have occasion to receive that? A. Yes.

Q. And did you conduct an analysis of the contents of that? A. I examined it for thiamine.

* * * * * * * * *

Q. And just explain what you did. [91]

A. Well, I followed the procedure described in the U. S. Pharmacopoeia, with modifications for this type of product.

(Testimony of Hubert H. Capps)

Q. Speak up louder.

A. The Thiachrome procedure for thiamine described in U. S. P.

Q. Did you have before you Government's Exhibit 7, the label of this product Pluri-B, in conducting your examination?

The Court: Did you have the label or had you seen the label?

The Witness: The label was attached to this bottle, I believe.

The Court: The witness refers to Exhibit 6 for identification.

* * * * * * * * *

A. Exhibit 6 and Exhibit 7. Exhibit 6, at the time I examined the sample, was on the bottle or attached.

* * * * * * * * *

Q. By Mr. Neukom: Is there anything on this label now of your markings?

A. Yes. I have my initials on the label.

Q. Indicating the black ink?

A. The date of examination and my initials. [92]

Q. "9-24-45 H. H. C.", is that correct?

A. That is correct.

Q. You will observe that the label says "Thiamine Hydrochloride—50 Mgms."—milligrams that is, isn't it?

A. Yes.

Q. And above that it says: "Each cc contains," and then the list of the various products, is that correct?

A. That is right.

(Testimony of Hubert H. Capps)

Q. Now, you conducted a test of this product which came to you, and in doing so did you ascertain whether or not each cc did contain 50 milligrams of thiamine hydrochloride?

A. My examination showed that this product, at the time I examined it, contained 33 milligrams per cubic centimeter, approximated.

* * * * * * * * *

Q. 33 instead of 50? A. That is right.

Q. Is thiamine hydrochloride, excepting when exposed to extreme high temperatures, is it reasonably a stable product?

A. In a properly made solution it is stable.

Q. Did you note whether or not this solution, in your examination, was in an oil base or a water base or what type of base? [93]

A. It was possible to mix it up with water and it dissolved completely in water, the solution did, so it was in a solution that is miscible with water. Presumably it was water.

Q. It was not then in an oil base?

A. It was not an oil.

Q. You examined the product in September, is that correct. A. 9-24-45.

* * * * * * * * *

Q. Now, assuming that the product received ordinary and reasonable care, and was not exposed to excessive heats, such as heats any more than would be normal from shipping and the weather, and basing upon what you found on September 24, 1945, the amount of the

(Testimony of Hubert H. Capps)

B-1 or thiamine chloride that you found, have you an opinion as to what percentage or what amount that product, substance, or solution had on or about July 16, 1945, the date it was originally shipped?

A. I believe it did not contain as much as 50 milligrams; not more than 33.

Q. Your opinion is then it contained about 33?

A. 33 milligrams per cubic centimeter.

Mr. Neukom: That is all. Counsel may cross examine. [94]

Cross Examination

By Mr. Stick:

Q. Where did you conduct this examination?

A. In my laboratory in Washington.

Q. Day time or night time?

A. Well, in the day time.

Q. Is there a name to the test that you used, like there have been to some of these others?

A. We ordinarily call it the Thiachrome procedure.

* * * * * * * * *

Q. What do you mean by a Thiachrome procedure? What is the procedure?

A. Do you want me to go into detail in it?

Q. Yes; I do. A. Complete detail?

Q. Thiachrome—"chrome" has to do with color, doesn't it? A. Well, yes, usually.

Q. And this procedure is a procedure that is carried out by the matching of colors; is that true?

A. No; it is not. The thiamine in the solution is converted into a material called thiachrome. This material

(Testimony of Hubert H. Capps)

flouresces and the flourescence is measured, and from the amount of flourescence we know the amount of thiamine that [95] was present in the beginning.

Q. And how is this flourescence measured?

A. We have a flourometer for measuring it. It is an electrical instrument.

Q. Does it measure or is it measured by a comparison of colors between the substance and a known standard?

A. We have a standard thiamine solution and we measure the amount of flourescence from that standard thiamine solution; and we also have a solution of this material that we are examining and we measure the flourescence from that material, and we compare the flourescence of the two and get our results.

Q. Now, just what do you mean by "flourescence"?

A. With a material that will flouresce, if a light of shorter wave length is passed through a solution, for instance, a thiachrome, a light of a longer wave length will be emitted, and we measure that light that is emitted.

Q. What is the accuracy of tolerance in that test?

A. The test with a solution like this would give us about five per cent, not more than five per cent difference.

The Court: Do you use the same quantity of the solution for the standard as you do for the material under examination, the substance under examination?

The Witness: We dilute them up so that the standard will have the same quantity of thiamine to begin with as our [96] sample. Both of them are diluted up in order to get the same amount of thiamine. We have to dilute them in the same way. Now, when the—

* * * * * * * * *

(Testimony of Hubert H. Capps)

The Court: What you are searching for is the amount of thiamine, isn't it?

The Witness: That is right.

The Court: What do you mean by "we dilute them up until we get the same amount of thiamine"?

The Witness: Our standard solution contains one milligram or one microgram of thiamine per cubic centimeter.

* * * * * * * * *

Mr. Stick: What is this you have in your hand?

A. These are my notes that I made at the time of the examination.

Mr. Stick: All right.

A. The standard solution was diluted up so that it [97] contained one microgram of thiamine per cubic centimeter. The Pluri-B was diluted also so that it would contain one microgram of thiamine per cubic centimeter, assuming that it contained 50 milligrams of thiamine originally.

The Court: As stated on the label?

The Witness: As stated on the label. Then when the thiamine was converted into thiachrome—

Q. By Mr. Stick: In each instance?

A. In each instance, both in the standard and in the sample, the readings were made for the flourescence, and it was less for the sample than it was for the standard solution.

The Court: Presumably they would be the same?

The Witness: Presumably they would be the same if the sample originally contained 50 milligrams of thiamine per cubic centimeter.

(Testimony of Hubert H. Capps)

The Court: Were both solutions in the same type of container?

The Witness: They were treated as nearly as possible exactly the same.

* * * * * * * * *

Q. By Mr. Stick: At the time you took the solution which is in the bottle before you, Exhibit 6, and diluted [98] it, there were in that dilution also other substances, were there not?

A. The label states that the product contains riboflavin, pyridoxine hydrochloride, pantothenic acid, and nicotinamide.

Q. And they were in the solution that you diluted?

A. Necessarily.

Q. Did you make any test for riboflavin?

A. No.

Q. For pyridoxine hydrochloride? A. No.

Q. Pantothenic acid did you test for?

* * * * * * * * *

A. No.

* * * * * * * * *

Q. Nicotinamide. Did you make any test for that?

A. No test.

The Court: You had thiamine hydrochloride. Say this solution that you were examining, Pluri-B, contained other ingredients and other properties, did you make an allowance for those?

The Witness: Do you mean, for instance, the riboflavin, pyridoxine chloride, pantothenic acid and nicotinamide? [99]

(Testimony of Hubert H. Capps)

The Court: Yes. Was your standard solution comprised of the diluting solution and the thiamine hydrochloride alone?

The Witness: Yes; the standard is.

The Court: Then your solution under examination is composed of thiamine hydrochloride and your diluting solution, plus these other items that are mentioned on the label which is Exhibit 7 for identification before you there?

The Witness: That is right.

The Court: In making the test do you make any allowance for the fact that the solution under investigation contains other properties than the standard solution contains?

The Witness: During my time with the Food and Drug Administration I examined probably 2,000 samples that some of them had the other ingredients present, for instance, riboflavin, nicotinamic acid, pyridoxine, and things of that kind, and I never could find any difference. It didn't make any difference whether they were present or whether they were not present as far as the thiamine was concerned.

The Court: This flourescence test, is it based upon a reflection of light that the presence of thiamine hydrochloride will make or cause?

The Witness: Yes. The light, the flourescent light, is generated, you might say, by the light that falls on the solution of thiamine. [100]

* * * * * * * * *

The Court: Will the presence of riboflavin change that color?

(Testimony of Hubert H. Capps)

The Witness: In the solution that we actually measure, the solution or thiachrome that we actually measure, there would not be any riboflavin present.

The Court: Well, I mention that only by way of example. Assume the presence of all or any of the other materials that are mentioned on the label, Exhibit 7 for identification.

The Witness: I will go a little more into detail in the procedure. These solutions are made up, and then after the conversion into thiachrome and before the measurement is made, the thiachrome is extracted with an isobutyl alcohol, and the other items, pyridoxine, riboflavin and nicotinamic acid would be left behind in the water solution.

The Court: So when it comes to the actual test of the two solutions, the standard solution and the solution under investigation have the same chemical properties, is that correct?

The Witness: As nearly as possible.

The Court: I mean quality, not quantity?

The Witness: That is right.

The Court: That is all I have.

Q. By Mr. Stick: At the time you received the vial or [101] bottle, Exhibit No. 6, did it have the cap on that it has now?

A. It did, or one very similar to it; and since this does not appear to be broken, I think that it did have that identical cap.

Q. And did you make any examination of that cap to determine whether or not it was punctured in any way, other than just looking at it? A. No.

Mr. Stick: That is all.

Mr. Neukom: That is all. May I offer in evidence the vial, if I have not already? I don't think I have. 6 and 7, may I offer into evidence, your Honor?

The Court: Exhibits 6 and 7 for identification are received into evidence. [102]

[GOVERNMENT'S EXHIBIT NO. 7]

30 cc STERILE SOLUTION No. 256
PLURI-B
(Some factors of the B Complex)
For Intramuscular Use
EACH CC CONTAINS:

Thiamine Hydrochloride	50 Mgms.
Riboflavin	1 Mgm.
Pyridoxine Hydrochloride	10 Mgms.
Pantothenic Acid	10 Mgms.
Nicotinamide	50 Mgms.

Chlorobutanol (Chloroform deriv.) 1/12 gr.—0.005 Gm.

CAUTION: To be used only by or on the prescription of a physician.

PASADENA RESEARCH LABORATORIES, Inc.
Pasadena 8, Calif., U. S. A.

Lot No.

[Written]: 29953 H. 8-30-45 F.A.G. 9-14-45 ONK 9-14-45 HWF 9-24-45 HHC

Case No. 19223. U. S. vs. Pasadena Laboratories. U. S. Exhibit 7. Date 6/18/47. No. 7 in Evidence. Clerk, U. S. District Court, Sou. Dist. of Calif. L. J. Somers, Deputy Clerk.

No. 11690. United States Circuit Court of Appeals for the Ninth Circuit. Filed Aug. 25, 1947. Paul P. O'Brien, Clerk.

* * * * * * * * *

DEFENDANT'S CASE IN CHIEF

RUSSELL R. BAVOUSET,

a defendant herein, called as a witness by defendants, being first sworn, was examined and testified as follows: [121]

The Clerk: Please state your name.

The Witness: Russell R. Bavouset.

* * * * * * * * *

Direct Examination

By Mr. Stick:

Q. What is your occupation, Mr. Bavouset?

A. I am general manager of the Pasadena Research Laboratories.

Q. How long have you been with that organization?

A. This is the sixth year.

Q. What are your duties there, generally?

A. Overseeing the production of materials.

Q. The production is made under your direction?

A. Yes, sir.

Q. What is your education and experience with reference to the manufacture of—what do you call it, biological preparations? [122]

A. Yes, sir. Well, this is my 20th consecutive year in the business. I have studied general chemistry and organic chemistry. I had some work in technology, etc., but most of my work has been practical, under Dr. E. S. Miller for 13 years, Dr. Simonson, etc., those people that I have worked with.

Q. In that time you have been in the work of manufacturing various preparations such as the ones that are referred to herein? A. Yes, sir.

(Testimony of Russell R. Bavouset)

Q. How long have you been making these preparations that are referred to in the information?

A. I believe the Vitamin B-1 products have been in existence now something like 10 years. I have been making solutions of Vitamin B-1 and B-complex solutions 10 years.

Q. And Vitamin D?

A. Vitamin D (in oil) is a relatively new product, that is, the injectable Vitamin D (in oil); and I believe the first we made of that was late in 1945.

Q. And the Indoform?

A. Indoform is an aqueous extract. We have been making that—I have been making that over a period of about 15 years.

Q. By "aqueous extract" what do you mean with reference to Indoform? [123]

A. Aqueous extracts are generally made with either raw glands or dessicated glands, and they are extracted with water under septic conditions, and after a period of time they are processed to eliminate unfavorable materials, and bottled and sterilized and put on the market.

Q. I will show you Government's Exhibits 3 and 4, 3 being a vial and 4 being the label taken from that vial, the labial vial called "Indoform." It has been alleged here that that was shipped from your laboratory on September 17, 1945. Is this matter manufactured in quantities of single vials or in quantities of a number of vials?

A. In quantities of a number of vials.

Q. And who manufactured the particular product that was contained in the bottle before you? A. I did.

(Testimony of Russell R. Bavouset)

Q. Will you state your procedure in the manufacture of that?

A. In the manufacture of this particular preparation an aqeuous—that is water—as the extractive is used and a flask containing whole ovarian, another containing anterior pituitary, and another containing thymus, thyroid, and lymphatic were all extracted separately, after which time they were filtered off and given the usual process of freeing that of foreign proteins and undesirable factors, combined and reduced to amount, and then suprarenal cortex from a concentrate [124] was added, and finally a posterior pituitary, and made up to the required volume containing the preservatives.

Q. And then the substances were placed in vials?

A. That is correct.

Q. And the vials were shipped out to the several parties as referred to in this particular instance, Dr. Joseph C. Bunten in Cheyenne, Wyoming? A. Yes.

Q. And this was one of several that were shipped to him. At the time that that was shipped was there three international units of p*ot*erior pituitary in a cubic centimeter of the contents of that bottle?

A. Yes. I measured out that amount for this particular solution.

Q. And was there one grain of thyroid substance in that matter at that time?

A. There was aqueously extracted one grain per cc of thyroid.

Q. Would that be the substance that contains iodine?

A. No, sir.

Q. Is the iodine substance of thyroid or thyroxine soluble or extractable in water? A. No, sir.

(Testimony of Russell R. Bavouset)

Q. There are other substances in thyroid than the iodine or thyroxine? [125]

A. There seems to be. Doctors request it.

Q. And you sell this preparation to doctors?

A. We do.

Q. And only to doctors? A. That is correct.

Q. They order it direct from you?

A. They order either direct by mail or through one of our salesmen.

The Court: What do you mean by "thyroid substance"?

The Witness: You take the powdered thyroid, that is the dessicated thyroid, and put it into a flask containing water, a measured amount of water, and that is extracted by shaking it over a period of time, usually two weeks. That is not continuously shaken, but several times a day, shaken up thoroughly and allowed to stand and then filtered off, and that material which is soluble in the water is then put into vials, with due process of sterilization, etc.

The Court: Then this Indoform did not purport to contain any iodine?

The Witness: No, sir.

The Court: What is the thyroid substance here it did purport to contain?

The Witness: Your Honor, I do not know the type of material that is designated therein. We put a disclaimer on that product, stating that it did not contain therapeutically [126] useful constituents, to definitely let the doctor know that the thyroid content was not the iodine content.

(Testimony of Russell R. Bavouset)

The Court: In the trade would the term "thyroid substance" have any particular meaning?

The Witness: In the trade the words "thyroid substance" for oral administration would mean the whole gland, that is, of course, meant to feed it or made ready for oral administration.

The Court: And that would contain iodine?

The Witness: Yes, your Honor; that would contain iodine.

Q. By Mr. Stick: In an aqueous solution would it contain that? A. No, it would not.

The Court: Is there anything on this label, this Indoform label, to indicate it is an aqueous solution?

The Witness: I do not believe so, your Honor. I believe we merely take that for granted, that it is an injectable, sterile injectable, and by its physical appearance is of aqueous nature.

The Court: Are there any words or symbols on the label which would tell a physician that this was an aqueous solution?

The Witness: I do not believe so, your Honor. The words "30 cc" would state that it was a solution, but not necessarily aqueous.

The Court: Of course, the fact it was liquid would indi- [127] cate a solution, too.

The Witness: Yes, sir. I believe, other than that, there is no indication.

Q. By Mr. Stick: Is thyroid substance in the form of thyroxine administered by injection?

A. I am not acquainted with any such preparations. There may be.

(Testimony of Russell R. Bavouset)

Q. Is the water-soluble extract administered by injection?

A. Yes; the water-soluble extract is administered by injection.

Q. I will show you the next combination of exhibits 6 and 7 of the Government.

The Court: Before you leave this thyroid question, I would like to ask the witness: Is there any other article on the market that you know anything about that has a label which specifies "thyroid substance" that does not contain any iodine?

The Witness: Yes, your Honor; there are many such preparations similar to this one and with thyroid, alone; that is, there is thyroid substance by itself without other materials in with it. There are many such preparations on the market, used daily.

The Court: That contain no iodine?

The Witness: Yes, your Honor. [128]

The Court: Sold to physicians?

The Witness: Yes, your Honor.

Q. By Mr. Stick: Do you have any of those substances? A. Yes; we do.

Q. Here?

A. I do not believe I brought anything like that along. I do not think I have a vial of thyroid substance here.

Q. Just plain thyroid substance?

A. Yes. I do not believe I have anything like that here.

Mr. Stick: If this matter goes over until tomorrow, will he be permitted to bring some of it in to show your Honor, and may I recall him at that time for that purpose?

(Testimony of Russell R. Bavouset)

The Court: Yes. He stated there are such. Unless the Government wishes to rebut it, I don't know whether there will be an issue as to that or not.

Mr. Stick: I see. Looking at Exhibits 6 and 7, 6 being a bottle and 7 being the label, that bottle—that is the correct combination, it it not, Mr. Neukom; 6 and 7 together is Count II?

Mr. Neukom: Counts III and IV, isn't it?

Mr. Stick: Or, Counts III and IV; yes.

Q. That label bears the mark "PLURI-B." That material was manufactured at your plant?

A. Yes; it was. [129]

Q. And by whom?

A. Probably by myself or—may I have that date?

Q. That was shipped 7-16-45, July 16, 1945.

A. It was probably made by myself.

Q. Made by whom?

* * * * * * * * *

Q. And will you state how that was made?

A. Those vitamins there are all aqueous soluble, that is, water soluble, and a combination is usually weighed out; that is, first, we weigh the thiamine chloride, Pyridoxine hydrochloride, and the calcium pantothenate in separate containers. The calcium pantothenate is converted into pantothenic acid, then the thiamine and pyridoxine and pantothenic acid are combined in one solution; then the riboflavin and the nicotinamide are combined in another solution, and it takes heat to put the riboflavin in. The nicotinamide is instrumental in putting riboflavin in solution. It is many times more soluble with nicotinamide present. So they are combined together and heated until

(Testimony of Russell R. Bavouset)

dissolved, after which time the pH. is adjusted to meet the pH. of thiamine and pyridoxine, approximately a pH. of 3.2. Then they are added together and processed with a glandular substance added in. A process for the purpose of eliminating any foreign material that might come down is gone through, chiefly bringing to boiling for 10 minutes and ice boxing for 48 hours. [130]

Q. Thus all of the matters set forth in the label there are combined into that solution? A. Yes, sir.

Q. And that, too, is mixed in amounts larger than that of a single vial? A. That is correct.

Q. And then the matter is put into these vials under 30 cubic centimeters to the vial?

A. That is correct.

Q. And at the time that solution is bottled does it have the full strength and potency that is set forth on the label? A. It does.

The Court: Have you had considerable experience in dealing with thiamine hydrochloride?

The Witness: Yes, your Honor; about 10 years.

The Court: Does it deteriorate in the bottle?

The Witness: Well, under certain conditions it does, your Honor.

The Court: What are those conditions supposed to be?

The Witness: Well, there are conditions such as where the pH. is not correctly adjusted, where the glass is not properly prepared ahead of time, that is, the vial that it is put in is not properly prepared ahead of time. There are deteriorating factors such as foreign particles that might be [131] introduced into the vial. There are deteriorating factors such as light and heat, exposed to air over a period of time.

(Testimony of Russell R. Bavouset)

The Court: But if this solution containing a certain quantity of thiamine hydrochloride is put in one of your bottles and sealed, is there any reason why, if it were examined six months later, it would contain any less than you put into it?

The Witness: I am not personally too familiar with that particular aspect. I could not say definitely one way or another.

The Court: What would be the situation with respect to posterior pituitary?

The Witness: There are certain factors that could cause that to deteriorate.

The Court: What would those be?

The Witness: Well, I would prefer to allow our gentleman who takes care of that explain it, as I am not as familiar with that as he is. [132]

* * * * * * * * *

Q. To go back a moment, again, to the Exhibits 6 and 7, the Pluri-B, I will ask you at the time that was made was [133] there an override of any of the material used in the manufacture of that?

A. I believe at that time we were using about five per cent override.

Q. Of what? A. Thiamine hydrochloride.

Q. Why?

A. Thiamine hydrochloride, in processing, has a very definite tendency to become impotent; it breaks down. It is a product that has certain deteriorating factors in it, and when handled it does break down. There are two types or possibilities of break down of that particular material. One will break down in heat, the other will break down in cold; and thus, as the break downs are

(Testimony of Russell R. Bavouset)

natural, to the detriment of thiamine chloride and natural to the Vitamin B product itself.

Q. And for that reason you put in this override?

A. That is correct.

The Court: Do you know of any danger of putting too much thiamine hydrochloride in that product?

The Witness: No, your Honor. There is very, very little toxic effect of thiamine hydrochloride in four times and up that particular strength.

Q. By Mr. Stick: The fact is that these vitamins are foods, are they not? [134] A. That is correct.

Q. Vitamin B-1 is found in the foods that we eat normally, is it not? A. That is right.

Q. Now, I show you Government's Exhibits Nos. 1 and 2, I believe they are.

Mr. Neukom: Those are the ones you have there. Do you want the label?

Q. By Mr. Stick: The one being two bottles in a box, and two being labels from those bottles; and they are marked "Pluri-B." Were these manufactured in your plant? A. Yes; I understand they were.

Q. How were they manufactured and under whose supervision? A. Under my own.

Q. These products are part of a shipment that is in evidence as having been made on June 18, 1946, to Dr. Ryerson in Phoenix, Arizona. It was part of a shipment?

A. That is right.

Q. Do you recall how much the original shipment was?

A. I believe the original shipment was about 50 vials.

(Testimony of Russell R. Bavouset)

Q. Will you state how that product was made? By the way, is that the same product as the other Pluri-B that we have here?

A. It is the same product, with one exception. Ribo- [135] flavin has been increased to two milligrams, instead of one milligram as the previous product.

Q. This product here has two milligrams of riboflavin? A. That is right.

Q. And the one in Exhibits 6 and 7 has one milligram? A. That is right.

Q. And other than that they are manufactured in the same way and contain the same ingredients?

A. That is correct.

Q. And were manufactured in lots larger than the one bottle or two bottles, and then were bottled and shipped? A. That is right.

Q. In the 30 cc vials? A. Yes, sir.

Q. I will ask you to look at the two bottles in Exhibit 1, look through them. Do you see anything in those bottles other than the liquid solution?

A. Yes; there is a precipitate.

Q. Was that precipitate in those bottles at the time you made it? A. No; it was not.

Q. Or when you finished making it?

A. No; it was not.

Q. Was that precipitate in those bottles when you shipped it to Dr. Ryerson on June 18, 1946? [136]

A. No; it was not.

(Testimony of Russell R. Bavouset)

Q. Before any of these materials are shipped have you any means in your office of checking these products?

A. We keep control batches for a short time after the material has gone out of the business, or the place of business.

Q. Are there any inspections made at the time they are shipped out?

A. Yes; a very careful inspection is made the last thing before it is placed in shipping cartons and sent out and marketed.

Q. By whom is that inspection conducted?

A. Well, we have one young lady at the head of the stock department, Mrs. Evelyn Smiley. There is another young lady, one of two assistants, that would likewise inspect this material before it goes out.

Q. And who is this young lady in charge of the shipping department? A. Evelyn Smiley.

Q. And she is here? A. She is. [137]

* * * * * * * * *

Mr. Stick: If it please the court, I have a young lady from the laboratory here whose testimony will take but a few minutes. It is agreeable to counsel for the plaintiff that I may call her out of order, if your Honor has no objection.

The Court: No. You may call her. Had you completed the direct examination of Mr. Bavouset?

Mr. Stick: No, I had not.

(Witness withdrawn.)

EVELYN M. SMILEY,

called as a witness by defendants, being first sworn, was examined and testified as follows:

The Clerk: Please state your name.

The Witness: Evelyn M. Smiley.

Direct Examination

By Mr. Stick:

Q. Mrs. Smiley, what is your occupation?

A. I am head of the shipping department.

Q. Where?

A. At the Pasadena Research Laboratories. [138]

Q. How long have you been with the Pasadena Research Laboratories?

A. It will be three and one-half years very shortly.

Q. You went with them in the year 1944?

A. That is right.

Q. And have been with them ever since?

A. Yes.

Q. How long have you been in charge of the shipping department? A. About three years.

Q. Were you in charge of the shipping department on the 18th of June, 1946? A. Yes; I was.

Q. And you were there at the laboratory at that time?

A. Yes, sir.

Q. What are your duties there?

A. Well, I received the invoices and the sale order and a shipping label from the office and clip those together with the packing slip. Then I go to the stock shelves and fill the invoice from the stock shelves. Then I take the orders, put my initials on the packing slips, check the vials, the solution in the vials, to be sure there is no foreign particles, before I put it on the invoice

(Testimony of Evelyn M. Smiley)

on the other table for the next girl to package and box and ship out.

Q. Now, the next girl who boxes for shipping, is she [139] under your direction? A. Yes; she is.

Q. Do you supervise her work? A. Yes.

Q. She puts the same boxes in the shipping package that you have selected and have examined? A. Yes.

Q. And then after they are put in the shipping package they are sent by parcel post? A. Yes, sir.

Q. And who sends them by that? A. I do.

Q. I will show you Plaintiff's Exhibits 1 and 2, 1 being two bottles of a substance called "Pluri-B", 2 being the labels from those bottles. I state to you that they were, by the evidence, shipped to Dr. Ryerson in Phoenix, Arizona, on June 18, 1946. Those bottles went through your selection and packing? A. Yes, sir.

Q. I will ask you to examine those bottles and state if you see anything in the contents of them other than this liquid?

A. Yes; I do. There are foreign particles.

Q. Were those foreign particles in there at the time that you selected them and tagged them? [140]

A. They were not.

Q. You examined for that purpose? A. Yes.

Q. You examined all of them for that purpose?

A. Yes.

Q. How long after you pack them is it that you send them by mail?

A. Usually I start packing about 8:30 in the morning and we take the packages to the post office about 4:30 at night.

(Testimony of Evelyn M. Smiley)

Q. So that they are mailed that day, the same day they are packed? A. Yes.

Q. Might it occasionally be that they are mailed the next day? A. Very seldom.

Q. Would that be mailed later than the next day, at any time? A. No.

Mr. Stick: Take the witness.

Cross Examination

By Mr. Neukom:

Q. What is your name, again? I didn't get that.

A. Evelyn Smiley. [141]

Q. Mrs. Smiley. Mrs. Smiley, you have a distinct recollection of having examined 50 bottles on June 18, 1946. Is that just because it is generally your habit to look at the bottles?

A. Well, I very seldom have an order that large. I think I could say that I remember the order.

Q. Well, you think you can say. Do you definitely recall this particular shipment?

A. No; I would not say definitely.

Q. You make a great many shipments, do you not, of vials of like size and all? A. Yes.

Q. Mrs. Smiley, for what reason did you examine to see if the particles were in there? You have been with this concern about three and one-half years, have you not? A. Yes.

Q. And haven't you found that, or have you found that, in most instances the sterile solutions were free of particles such as you note here? A. That is right.

Q. Then it would be rather unusual to find them; would that be it? A. Yes.

(Testimony of Evelyn M. Smiley)

Q. But you had found them in the past?

A. Occasionally; yes. [142]

Q. And that is the reason why you think you recall looking on this date here?

A. No. It is just force of habit, I would say. I always look at them. I never box anything unless I do look at it.

Q. What do you do; do you put them up to some light that you have there? How do you go about that?

A. We have an inspecting lamp, and then we have a light over the table that I package on. I always hold it up to the light before I select and put it in the box.

Q. Your best recollection, that you are definite on it, is that none of the 50 had any particles in them when you shipped them? A. No, sir.

Q. But you have seen particles in other batches of similar material there at the plant; is that true?

A. I have found some.

Q. What have you done about that?

A. We always take it back upstairs.

Q. Have you ever told Mr. Bavouset about finding undissolved particles in sterile solutions?

A. Yes, sir.

Q. When do you recall having told him that?

A. Oh, I would say about two weeks ago.

Q. And was that also in a sterile solution? [143]

A. Yes.

Q. And have you found undissolved particles in any of the other products that were sold for intravenous or intramuscular injections? A. Very few.

(Testimony of Evelyn M. Smiley)

Q. Is there a chemist there or a pharmacist that you have also talked to about finding such a thing, such a foreign particle?

A. I always spoke to Mr. Bavouset about it.

Q. Mr. Bavouset really sort of controls the whole concern, is that correct? A. Yes.

Q. He hires you and was in charge of your duties?

A. Yes.

Q. Is that right? A. Yes.

Mr. Neukom: I think that is all.

Redirect Examination

By Mr. Stick:

Q. Was it your instructions from Mr. Bavouset when you assumed your duties there to make these inspections?

A. Yes.

Q. Invariably? A. Yes. [144]

Mr. Stick: That is all.

Mr. Neukom: Just one question.

Recross Examination

By Mr. Neukom:

Q. They were labeled when you examined, weren't they? A. Yes.

Q. The labels went around about half of the bottles, didn't they?

A. I can always see plainly what is in it, even though the label is on it.

Q. The label such as reflected here on Government's Exhibit No. 2, this label went around the bottle as far as it would go around, is that correct? A. Yes.

Q. And was glued on there? A. Yes.

(Testimony of Evelyn M. Smiley)

Q. And you did not know when these bottles had been manufactured or bottled; you just knew that they were in stock and you went to the stock and procured them and looked at them and had them packed, is that correct? A. Yes. [145]

* * * * * * * * *

RUSSELL R. BAVOUSET (Recalled)

Direct Examination (Resumed)

By Mr. Stick:

Q. Mr. Bavouset, you have known Mrs. Smiley who was just on the stand preceding you?

A. Yes; I do.

Q. She has been in your laboratory, she said, since 1944; that is correct? A. That is correct.

Q. At the time she took charge of the shipping department what instructions did she have with reference to inspection of materials?

A. Before any of the material may be packed after it is taken off the stock shelf, it is to be inspected very carefully.

Q. You gave her that instruction?

A. I did. [146]

Q. That was an invariable part of your procedure in your laboratory? A. Very definitely.

Q. Is that standard practice in other laboratories where you have worked?

A. Yes; it has always been standard practice.

Q. In the laboratories in which you have worked?

A. In which I have worked; yes.

(Testimony of Russell R. Bavouset)

Q. Have you ever visited other laboratories than those in which you have worked?

A. Well, I have visited several locally, but as to whether that was standard practice there I couldn't say.

Q. Do you know whether they performed or went through with the same practice there?

A. I know that they inspected them very carefully. Whether it was just before they were packed I couldn't say.

Q. That is in those that you were not working in?

A. Yes, sir.

Q. Do the inspectors of the Food and Drug Department come to your laboratory? A. Yes; they do.

Q. And have over what period of time since they first came there, approximately?

A. Oh, I believe the first appeared there very shortly after we started in business, say, five years ago. [147]

Q. Did they make any inspections of the plant?

A. Yes. I believe about once a year they go through the plant very thoroughly.

Q. How often do they come there, in general?

A. Well, sometimes they would come as often as once that month, and sometimes once in three months, sometimes even less frequent.

Q. Did they at any time ask to see your books and shipping records? A. Yes; they do.

Q. What did you reply to them when they asked to see them?

A. Well, my first experience with the Pure Food and Drug inspector was, perhaps, four years ago. I asked one of the gentlemen there about his authority to examine our records and he assured me he had such authority.

(Testimony of Russell R. Bavouset)

Q. Did you ever ask any of the other inspectors that came there, besides him, whether they had any authority to inspect your records?

A. I have spoken to them about their authority, from time to time; yes.

Q. What did they say? [148]

* * * * * * * * *

A. They always assured me they had the authority to examine our records.

The Court: What records?

The Witness: Invoices which we file after the regular invoice has been shipped out.

The Court: You mean your office copy of the invoice?

The Witness: Yes, your Honor.

The Court: That is the invoice to the physician and customer?

The Witness: The duplicate invoice to the physician; [151] yes, your Honor.

Q. By Mr. Stick: And those were inspected by the inspectors? A. Yes, regularly.

Mr. Stick: Take the witness.

Cross Examination

By Mr. Neukom:

Q. Mr. Bavouset, none of the inspectors took any products from you that have been offered here in evidence, did they? A. No, sir.

Q. So far as you know, they obtained all of those from people that you had freely and willingly mailed the product to, did they not? A. As far as I know.

(Testimony of Russell R. Bavouset)

Q. And you had no objections to any of your customers turning over to the Food and Drug inspectors any of your product, had you?

A. No; I had no objection.

Q. Your product was open on the market, and if I had walked in there and said I was a doctor and wanted to buy your products, you would have sold them to me, wouldn't you?

A. I would have sold them to any ethical medical doctor. [152]

Q. And if any food and drug inspector had come up and told you he would like to have bought a product, because he wanted to make an analysis of it, you would not have objected at all?

A. I would had it been a product of ours.

Q. Objected to the food and drug officers having your product to make a proper inspection or analysis?

A. They wouldn't have done that, because it is not within the state; so I know that they wouldn't want anything of that kind.

Q. You would have objected to that, though, would you, Mr. Bavouset?

A. Well, I couldn't say. I don't know of any reason why I should have.

Q. All right. Now, your product here, we will take the labels. You were responsible for these labels, were you not? A. Yes.

Q. For the contents of them? A. Yes.

Q. And you gave the labels some thought before you had them printed? A. Yes.

Q. For instance, if we will go to Pluri-B which is reflected on Government's Exhibit 2 in evidence, you

(Testimony of Russell R. Bavouset)

note that [153] it says "riboflavin 2 mgms." or two milligrams per cubic centimeter. Can you find anything on there which shows that that is in an aqueous solution?

A. Other than the fact that it says "sterile solution." It doesn't say "aqueous".

Q. There is nothing there to inform a doctor that it was in the type of solution that you have testified to, is there? A. No.

Q. And that is the substance which is reflected by the vials here, Government's Exhibit No. 1, a portion of Government's Exhibit No. 1; isn't that correct?

A. That is a portion.

Q. That was the label that was on?

A. Oh, yes. That is the type of label we would put on such a product.

Q. Now, thiamine hydrochloride, I think you state, does under some circumstances, according to your understanding, have some deteriorating faculties; that is correct, isn't it? A. That is right.

Q. You were selling this to doctors and you made this batch in the fall of 1945, did you not?

A. That is right.

Q. And you did not anticipate selling that batch within maybe one week or two weeks, did you? [154]

A. No.

Q. You intended to keep that amount or that amount that you had put up until in the current course of events it had been sold, or until it had been on your shelves for maybe too long, and then you would remove it, didn't you? A. That is right.

(Testimony of Russell R. Bavouset)

Q. And you kept it on shelves just like we see in drug stores, did you not? You did not have it in an ice box or anything like that? A. That is right.

Q. You expected that the doctor who would buy this product would take it out of this rather unique sponge rubber thing by the injecting device that he had, did you not? A. Yes; per the hypodermic needle.

Q. Per the hypodermic needle.

A. With a syringe.

Q. You were aware from your experience in manufacturing these products that a doctor might keep such a product as this for many months before he would use it, were you not? A. He might.

Q. You were aware of the fact that formerly, until this sponge rubber device was developed, that normally doctors used to buy many of their intravenous solutions in little ampules that they would break just to give one; that there would be just sufficient for one injection? [155] A. That is right.

Q. It was your contention that this, maybe, contained 30 to 40 times as much as any of these little ampules; isn't that true? A. Yes; that is right.

Q. And you anticipated that a doctor might have retained this bottle for some time until it had served its purposes; isn't that true?

A. That would be true.

Q. Now, did you think that it was important to caution the doctor about this product or any other product to the effect that this thiamine hydrochloride was a rapidly deteriorating product or was a deteriorating product?

A. It is not a rapid deteriorating product under ordinary circumstances, that is, in solution.

(Testimony of Russell R. Bavouset)

Q. Then you felt that it was sufficiently stable, that even a year after you had made it, it still ought to be in good shape and would be efficacious in the amounts as your label indicated; is that correct?

A. It might have deteriorated some. I would not say a great deal in that length of time. [156]

* * * * * * * * *

Mr. Stick: May I be permitted at this time to say that I would like to withdraw the position I took yesterday with reference to the authority of the inspectors to examine the records or the shipping receipts? I think it is only fair that I should do it at this time, so that I will not take up the time of the court.

Mr. Neukom: Thank you.

RUSSELL R. BAVOUSET (Recalled)

Cross Examination (Resumed)

By Mr. Neukom:

Q. Merely by way of example, Mr. Bavouset, would you look at the cork or the stopper, whatever it is called, for instance, on Government's Exhibit No. 8, and the plastic seal around this, and then it is sponge rubber. From your understanding and from your experience, using that as an example, is that not considered to be one of the latest or the most improved methods of corking and sealing products of all of the characters that are involved here? A. Yes; that is one of the methods.

Q. And that has proved to be quite satisfactory; that is to say, does not allow impurities to get in, to your [160] knowledge; isn't that correct?

A. Yes; that is.

(Testimony of Russell R. Bavouset)

Q. And retards light, of course, from getting in and keeps the contents in a reasonably good state of preservation; isn't that correct?

A. That is correct.

Q. And the bottle itself of the character of No. 8, and likewise the other bottles which, from appearances, are the same, is of an amber color; and I have noted and I believe and am going to inquire of you if it is not true, that it has been found that an amber colored glass of this character has a tendency to assist in retaining the quality of the product that is placed in it, does it not?

A. Yes; in those products where light causes damages.

Q. To your opinion, these bottles are of approved and most proper shape to be used in placing any one of these solutions that you were offering for distribution, are they not? A. I believe they are; yes, sir.

Q. Now, taking up the substance "Indoform" here, as I understood your testimony to be, that you placed in this vial when you made up the amount which was to be vialled—if that expression might be used—

The Court: Do you use that synonomously with "bottled"?

Mr. Neukom: "Bottled", that is the word I wanted and [161] it didn't come to me.

Q. About how many bottles or vials do you recall manufacturing shortly prior to the date of the shipping of the Indoform involved in this case?

A. That is the total number of vials manufactured up to this time?

(Testimony of Russell R. Bavouset)

Q. No; the amount that constituted the pre-bottling that went into the shipment of around September 17, 1945.

A. The amount that was made up at the time this particular material was made up, is that it?

Q. Yes; that is the point there.

A. I do not have the records on that. At that time, it seems to me that we were making between two and three litres at a time, or would run somewhere between 65 and 100 vials.

Q. And that product was mixed, or whatever its chemical work, was done by you, is that correct?

A. That is correct; yes, sir.

Q. And likewise, the product involved in this case, that is to say, the amount prior to the shipping of Pluri-B, as I recall, you likewise prepared that, did you not? A. That is right; yes, sir.

Q. And the product that is designated as "Vitamin D", you likewise handled the manufacturing or the placing together of the constituents there? [162]

A. Yes. The compounding, yes.

Q. Compounding, that is the word. And the product which is known here as the sterile solution, likewise, and Pluri-B, as I recall, in Count VII, you handled the making of that, the product which we now observe has the cloudy or precipitated particles in it?

A. That is right.

Q. May I just inquire, you are not a chemist, are you, Mr. Bavouset?

A. I am not a graduate chemist; no.

(Testimony of Russell R. Bavouset)

Q. But you have had years of experience, of course, in this kind of work, haven't you?

A. That is right.

Q. And have made a great many products, I assume, in those years of experience? A. That is right.

Q. You are likewise not a pharmacist, are you?

A. No, sir; I am not.

Q. Then, I take it you did not graduate from schools in either of those trades?

A. I am not a graduate of any university.

Q. I see. Our father was quite a good druggist, but neither was he a graduate of any university. May I inquire now, Mr. Bavouset, with respect to this Indoform again, as is reflected from Government's Exhibit No. 4? You [163] stated to me that the label was a matter which you had prepared; that is correct, isn't it?

A. That is correct.

Q. And you, of course, expected this label to be read by men who were trained in the medical field and who had knowledge of pharmacology or the constituents of various types of medicine or more recent foods which some of these B products are called; isn't that correct?

A. That is right.

Q. And when you used the term "thyroid substance" there, it was your understanding that the practicing physician and surgeon would naturally believe that that denoted a thyroid substance as might be reflected in the Pharmacopoeia; isn't that correct?

A. No; that is not.

Q. Well, now, do you know of any thyroid substance that a physician might care to use, even combined with

(Testimony of Russell R. Bavouset)

other compounds, that he would desire to use unless it had some therapeutic value?

A. Well, I have talked to doctors about this thing and I know that—they have expressed opinions about the activity, etc., and there is a great deal of variation in the minds of the doctors what is accurate and what is not. I am not a pharmacologist so I can't tell you straight off.

Q. Mr. Bavouset, the posterior pituitary, you know, has some therapeutic value, has it not? [164]

A. Yes.

Q. And the other essential or individual components of this product have? Whole ovarian, that was not a meaningless product, was it?

A. Well, I didn't manufacture it to be.

Q. It was your intent that it had some value to be used in the human body, was it not? A. Yes, sir.

Q. Now, when you used the words "thyroid substance" didn't you think it would be only proper and advisable for you to advise on your label the doctor that this was a product with negative value and did not contain any of the iodine constituents which are normally in the thyroid?

A. Taking into consideration the rules and regulations, I thought it would be advisable to advise them that way; yes, sir.

Q. Well, you have pointed out on the bottom of that label that all of the products apparently have no therapeutic value; isn't that correct?

A. In this particular solution, this form would not be measureable.

(Testimony of Russell R. Bavouset)

Q. Now, just what was it that the thyroid did contain, if it did not contain any of the iodine?

A. Well, as I say, there is a great deal of variation in the opinions of medical doctors, even in the medical [165] schools, as to what does compose thyroid. There is a measurable substance in thyroid known as thyroxin, and it is generally considered the active ingredient. But I have talked to many medical doctors who claim that there are other activities that can be attributed to thyroid other than the activity of the thyroxin itself.

Q. Isn't it true the iodine that is in thyroid is there from what—not I—the chemists consider an organic source, that is to say, it comes into it as a result of body action rather than from an artificial placement?

A. That is correct.

Q. That is true, isn't it? A. Yes, sir.

Q. And that it be free from an inorganic source, that is, taking the salt itself and placing it in, rather than nature doing it; isn't that correct?

A. That is right.

Q. Were you not familiar with the Pharmacopoeia which gives the definition of "thyroid", turning to page 503 of the 12th Edition? A. Yes; I was.

Q. And it reads, does it not: "Thyroid is the cleaned, dried and powdered thyroid gland previously deprived of connective tissue and fat." With that you agree, is that not true? [166]

A. That is correct; yes, sir.

(Testimony of Russell R. Bavouset)

Q. Did your thyroid gland have the connective tissue and fat in it, or do you know?

A. Well, all the material that I purchased was purchased already dessicated, and I believe it was well defatted. We checked the content, etc., and I am quite sure it was as described by the U. S. Pharmacopoeia.

Q. "It is obtained from domesticated animals that are used for food by man. Thyroid contains not less than 0.17 per cent and not more than 0.23 per cent of iodine in thyroid combination." Is that correct?

A. That is correct.

Q. "And must be free from iodine in inorganic or any form of combination other than peculiar to the thyroid gland." In other words, as I previously questioned you, it must be free of inorganic, coming from a foreign source, to be a thyroid substance; isn't that correct? A. To be a thyroid iodine it must be.

Q. And carrying on further: "A dessicated thyroid of a higher iodine content may be brought to this standard by admixture with a dessicated thyroid of a lower iodine content or with lactose, sodium chloride, starch or sucrose." You agree with that statement in the Pharmacopoeia, do you not? A. That is right. [167]

Q. And yet, Mr. Bavouset, is it not true, then, when you place on a label the designation "thyroid substance" that you are doing so, knowing that medical men will read that and will assume that the product contains the same as the definition of "thyroid" as is reflected in the Pharmacopoeia that I have just read to you?

A. I did not do it with that intention. I did not feel that that was the way it would be.

(Testimony of Russell R. Bavouset)

Q. You knew that the medical man obtaining this thyroid was not getting the thyroid with the iodine content?

A. The medical man who would take a solution of thyroid would ordinarily know, I am sure, that he would not have iodine present.

Mr. Neukom: Just my question again, if I may, and then you, of course, can explain it.

* * * * * * * * *

A. That is right.

Q. Now we will look at Government's Exhibit No. 4, as we did at some of the others yesterday. There is nothing on that label, is there, nor was there on the vial anything cautioning a doctor as to any unusual precautions which should be indulged in in relation to this product? A. No, sir.

Q. Now is there anything on the label telling the [168] doctor that any of the products might lose their efficacy with a reasonable period of time?

A. No, sir.

Q. This statement seems a little singular to me and I would like to have you explain it, if the court is interested: "This preparation does not contain any known therapeutically useful constituent." What was the significance of that statement?

A. Well, in the first place, the Pure Food and Drug rules and regulations made it necessary for any product that did not have a known standard, as set forth in some of our standard books, such as the United States Pharmacopoeia, national formula, etc., if they did not have a known standard, that it would be necessary to put a disclaimer on. This was followed throughout the

(Testimony of Russell R. Bavouset)

industry. First, as I remember, it was sold as "whole ovarian," and we would say, "no estrogenic precipitation present," etc. That form was changed several times. This particular statement here, being a disclaimer, meaning that we do not know of any particular test which would prove the potency of this product, was put on there for that purpose.

Q. But you were not selling it, of course, as an entirely futile product? I mean as just like a handler of distilled water, of course?

A. No. That particular statement was put on there [169] due to the fact that we were trying to conform to all rules and regulations and, at the same time, give the doctors what they wanted.

Q. In your opinion, this preparation "Indoform" reflected by the label of Government's Exhibit 4 for identification, if there were anterior pituitary 30 grains per each cubic centimeter in the product when you combined it, and had it received just normal care, temperatures of rooms and all, three months or six months from that, that same amount should have been in the vial, should it not? A. That is right.

Q. And it would not have deteriorated rapidly?

A. Yes. That is the anterior pituitary you are speaking about?

Q. Yes; referring to that and that alone.

A. Yes, sir.

Q. Referring to the thyroid substance, your answer would be the same as to that?

A. That is right; that is right.

Q. With respect to Government's Exhibit No. 2 for identification—I believe we covered this, but I will try

(Testimony of Russell R. Bavouset)

to hasten along—the Pluri-B, the thiamine hydrochloride-50 milligrams per each cubic centimeter, had there been that amount in there when you combined it, six months from then, had that bottle been retained, had the seal been retained on [170] there and no unusual factors entered into it, approximately that amount should have remained in the solution, should it not?

A. That is right.

The Court: Are you referring to Exhibit 2 for identification?

Mr. Neukom: I am referring to Exhibit 2 in evidence. I read the upper one but I did not look at the bottom, your Honor, and I will say that inadvertently.

* * * * * * * * *

Q. May I inquire, Mr. Bavouset, did you have any of the basic materials that went into any one of these four—I think there are three—three different solutions or compounds, prior to compounding the individual allotment or allotments, did you have them assayed? [171]

A. Other than labeled potency, as I purchased it from the manufacturer, I can think of but one that I had assayed, and that would be one that I made myself. That would be the posterior pituitary. I do not have the exact batch of material that I made at that time available; that is, I do not remember it, it has been so long ago. But at that time I was making the posterior and still am making the posterior pituitary myself, and at that time the biological process was completed and I then sent that assay out for a batch assay of the posterior pituitary itself. That is not an assay of the Indoform; that is just the posterior pituitary.

(Testimony of Russell R. Bavouset)

Q. But you do not recall whether the product that went into the Indoform reflected in Counts I or II here—

A. No.

Q. —was assayed prior?

A. Only as I said, the posterior pituitary, I know, when I used it was up to standard. I diluted that, of course.

Q. As a matter of fact you did not have that particular posterior pituitary assayed, did you, that went into this allotment here? A. Yes; I did.

Q. Have you brought that assay with you?

A. No. It would be impossible for me to say which batch went into it. In other words, I have a large batch of posterior pituitary which I make up, we will say, approximately [172] 20 units. I have that assayed and then use it on that basis.

Q. The finished compounded preparation of any of these three here, then, you can explain further, that if any of these four drugs here, including the sterile matter which has the suspended particles in it, did you have any assays conducted on any of the finished product?

A. Does that include that particular product there that has come down in precipitate?

Q. Yes; it includes that, too.

A. I unfortunately did not bring the assay card on that, as the matter of the potency was not involved here. I did not bother with it. The other products I did not have because the facilities were not available at that time. But I am quite sure I have an assay card on the material. It is all being assayed at the present time, and I am quite sure that I do have an assay card.

(Testimony of Russell R. Bavouset)

Q. That is a card back in 1945? Did you have an assay run on it shortly after you had compounded it?

A. No.

Q. Then you had sent the amount of it to Dr. Ryerson— A. Was that in 1945?

Q. I will get the date. '46. You had sent the quantity designated to Dr. Ryerson on June 18, 1946 prior to [173] conducting any assay upon the sterile solution of Pluri-B, had you not?

A. No; there was an assay run on that.

Q. Have you brought it with you?

A. No. I am sorry I did not bring it. As I said before, the amount of the matter of potency did not come up in that particular case.

Q. Didn't you think that would be rather important in connection with this matter, Mr. Bavouset?

A. I did not, inasmuch as the potency had not been involved.

Q. Weren't you concerned; weren't you getting any complaint, even, from Dr. Ryerson about the suspended particles in that matter?

A. No. Dr. Ryerson did not complain about that particular shipment.

Q. He did not complain directly? A. No, sir.

Q. The thiamine hydrochloride that went into this Pluri-B, as reflected from Government's Exhibit 2 for identification, did you have that assayed, the basic product? A. No, sir.

The Court: That is Government's Exhibit 2, the label?

Mr. Neukom: Yes, your Honor; the label.

(Testimony of Russell R. Bavouset)

Q. And did you have assayed the thyroid substance [174] that is contained in this Indoform? Did you have that assayed?

* * * * * * * * *

A. No, sir.

Q. Do you recall that you were present at a hearing, at an administrative hearing, of the Food and Drug Administration conducted in conjunction with this investigation, and appeared on or about November 7, 1945 before Mr. Rowe, the gentleman who is writing here, sitting next to me, and they were investigating a matter concerning some of these products here, and particularly the Pluri-B that is referred to in this case in Counts III and IV—this matter is not upon the file—didn't you state to Mr. Rowe at that time that your more recent investigation indicated that this particular shipment could have had a deficiency in Vitamin B-1, the thiamine?

A. I am very sory, I can't remember such a statement.

Q. Do you recall that you were present on or about April 23, 1946 in a Food and Drug Administration hearing conducted before Mr. Gray? Is Mr. Gray here? Will you stand up? Do you recall that gentleman?

A. Yes; I do.

Q. And that is with reference to the product which [175] became the subject matter of Counts I and II, the Indoform, and that you stated that you had had that solution later tested by the Cooper Laboratories who found it contained such small quantities of posterior pituitary as to be immeasurable?

A. That is right; I did that.

(Testimony of Russell R. Bavouset)

Q. And that is, of course, after you had shipped the product? A. That is right.

Q. And did you not likewise state to Mr. Rowe at the hearing on or about November 7, 1945 with regard to the Pluri-B and the thiamine deficiency, that you did not have the equipment to make the thiachrome determination for thiamine and that you would have to, therefore, revise your manufacture and procedure?

A. We did not have the equipment. Now, about the revision of manufacturing procedure, that goes on almost every day. [176]

* * * * * * * * *

Q. Is it not true that, with regard to the undissolved particles in this Government's Exhibit No. 1, the product shipped to Dr. Ryerson, that you yourself only examine for undissolved particles at the time that you make the product? A. No; that is not true.

Q. Mr. Bavouset, do you subscribe to the testimony as reflected by Dr. Wiley, that this product contained 20 times the amount of riboflavin—

A. I recall his testimony.

Q. Yes. —that can be hoped to be dissolved in an aqueous solution? Do you subscribe to the statement, or do you have a variable thought on that?

A. I would like to qualify it.

Q. Surely, you may. [177]

A. I have examined the products manufactured of all my competitors—not all my competitors, but many of them, and I believe, right in court today, we have one that contains four milligrams of riboflavin per cubic centimeter, in competition with our product, which would be 40 times. The fact that one-tenth—let's see; that

(Testimony of Russell R. Bavouset)

would be about one-tenth milligram per cc, soluble in ordinary water solutions, would have to be considered in the light that nicotinamide is a very fine solvent for riboflavin, and that when you put riboflavin in a solution with nicotinamide it will aid a good deal.

There are other substances, salts, that are recommended by the manufacturers of riboflavin. I have correspondence of those manufacturers that these salts aid the putting into solution and stabilizing in solution riboflavin.

That has been a major problem with all manufacturers, and much discussion and much writing has been done upon the subject.

The Court: Is it your opinion that the precipitate in those two bottles which are part of Exhibit 1—are they not Exhibit 1?

Mr. Neukom: Yes, your Honor; they are a part of Exhibit 1 and the label is Exhibit 2.

The Court: Is it your opinion that, whatever that substance appears to be precipitated in that liquid, is a [178] precipitate of riboflavin?

The Witness: Yes, your Honor; it is my opinion. I can't say that entirely, but that is my opinion.

The Court: And that would be due to the excessive amount of riboflavin over and above what would dissolve in the solution?

The Witness: Not necessarily, your Honor. That might be due to varying conditions of weather. I have noticed it come down upon fluctuation of temperature. Putting into warm water, very often that type of thing goes back into solution or remains that way. It is rather common. We have had that happen. Even some manufacturers go as far as to state on their label: "In case

(Testimony of Russell R. Bavouset)

riboflavin precipitates, warm until it goes back into solution."

Q. By Mr. Neukom: Then it is your position that nothing, of course, has been added to either one of these bottles other than what you put into them. Let us, you and I— A. I take that stand.

Mr. Neukom: Let us take the cork here and cut off this seal.

The Witness: I don't believe there is any reason for—

The Court: You are taking off the seal of one of the bottles comprising Exhibit No. 1?

Mr. Neukom: Exhibit No. 1, your Honor, so that we may see the rubber cap as well as we can. Of course, a little paper [179] adheres to it.

Q. But it has the indications, does it not, that nothing has been added to the product?

A. It has that indication. I couldn't say, of course, but I would take the stand that it does not have.

Q. And you do not advise, by your label or otherwise, the prospective user of this product that such a condition might accur?

A. No. I had not expected it to occur and for that reason had not advised them.

Q. What has been your experience as to how soon after the compounding of this product that that condition does occasionally occur?

A. Sometimes those vials will go for six, seven or eight months and then nothing ever occurs to them. Then sometimes we will get the refrigeration extremely low temperature, a break in the weather, that is, and a portion of the riboflavin content comes out in a precipitate.

(Testimony of Russell R. Bavouset)

Q. Could it be other impurities? It is riboflavin, or would you want to express an opinion?

A. I don't know. I really couldn't say. I don't believe so.

Mr. Neukom: I see. I think that will be all.

The Court: Would it be your opinion that a lesser amount of riboflavin would be less likely to precipitate? [180]

The Witness: Yes, your Honor; I would be of that opinion. As I have said, I have examined the products of many of my competitors and I have found that precipitates come out even in lesser amounts, that is, even in lesser concentrations, sometimes, and they still come out where, perhaps, the other type of salts that are good for stabilizing have not been used. I couldn't say what they are using, but sometimes a small amount of riboflavin comes out due to its insolubility, the same as a larger amount. It has been a major problem.

The Court: Is there some definite purpose in including in one of the Pluri-B products only one milligram of riboflavin per cubic centimeter and, in the other, two milligrams?

The Witness: Yes, your Honor. The intramuscular as I said, it was quite stable and we had a lot of success with it. And then we put in two milligrams. Perhaps I was a little optimistic, I don't know, and we had a great deal of good fortune with that at all times, and upon a very rare occasion something like this did happen.

The Court: I notice apparently that the label for the product containing only one milligram of riboflavin states that it is for intramuscular use, whereas the label of

(Testimony of Russell R. Bavouset)

the product Pluri-B which contains two milligrams of riboflavin states for intramuscular or intravenous use.

The Witness: Yes, your Honor. The intromuscular use [181] material here, the multiple dose vials, where they are punctured many times, that has been frowned upon for intravenous use by some physicians; and we had taken a stand that it was usually to be used for intramuscular use only.

Later on, it seems to have become very well recognized, at least it is common practice to use material from vials in intravenous use.

We checked to see if other manufacturers were using for intramuscular and intravenous use both materials where intravenous use may be indicated, and we found they were using that type of labeling; so we included that in our particular product.

The Court: What I was attempting to arrive at, what would be the reason for a product called Pluri-B, containing one milligram of riboflavin per cubic centimeter that would be labeled "for intramuscular injection," and another product, the same product, containing two milligrams or riboflavin per cubic centimeter, labeled "for intravenous or intramuscular"?

The Witness: There is really no reason for that, other than the fact that in the length of time between the two we had noted that our competitors were using it for both intramuscular and intravenous use, that is, similar products; and we felt that, inasmuch as it had become common practice, that we would include intravenous use as well. [182]

The Court: Is it your opinion that the Pluri-B with one milligram of riboflavin per cubic centimeter would

(Testimony of Russell R. Bavouset)

be just as efficacious as the same product with two milligrams of riboflavin per cubic centimeter?

The Witness: Yes; it would be.

The Court: And if it were to be used for intravenous injection, and there is danger of precipitation, it would be a safer product to have lesser riboflavin in it, would it not?

The Witness: Well, that is true to a certain extent, your Honor. I did not expect it to be that way, of course, originally.

The Court: Now with respect to the thiamine hydrochloride, would you expect if you put 50 milligrams in a cubic centimeter of product, would you expect it to dissipate in some way to where there would be only 33 milligrams per cubic centimeter a few months later, or even a year later?

The Witness: No, your Honor; I would not expect that.

The Court: Is there any reason you can think of why there would be less thiamine hydrochloride later than there was at the time it was manufactured?

The Witness: Well, those factors which have to do with the breaking down of thiamine, including the way it is kept, for one thing, the base, that is the alkaline or acid condition of the base in which it is in, anything that [183] influences that, then it breaks down much faster.

There are certain factors involved there that we do everything we can to take care of, and expect them under normal circumstances to remain constant.

(Testimony of Russell R. Bavouset)

The Court: Have you had any experience with thiamine hydrochloride in a solution dissipating to the extent of a third or a half?

The Witness: Yes; a great deal, your Honor. And making these solutions, if we approach the neutral stage, we will say, where we have a pH. as high as 7, the material is not stable at all and, with a small amount of heat, dissipates very, very rapidly. So, for that reason it is necessary to keep thiamin hydrochloride in concentration up around 3.2.

The Court: You have been making this Pluri-B for sometime?

The Witness: Yes, sir, your Honor.

The Court: Have you had any trouble with the thiamine hydrochloride content becoming dissipated?

The Witness: No; not in Pluri-B as long as we watch our pH.

The Court: Well, what would cause it to dissipate, exposure to air?

The Witness: Well, that exposure to air could cause the dissipation of thiamin, your Honor. [184]

The Court: If the doctor takes one of these vials or bottles and he punctures the cap, the rubber cap, with a hypodermic needle to make an injection in the patient today, then he has a patient requiring more treatment next week, and another one next month, and another one two months later, would you expect the recurring punctures in that cork, that rubber cork, will admit air and cause the thiamine hydrochloride to dissipate?

(Testimony of Russell R. Bavouset)

The Witness: Yes, your Honor; that is a known fact, it will be done.

* * * * * * * * *

The Court: Would this cap here, this rubber cap, be a safe cap to use on this product where it is punctured time and again by a hypodermic needle?

The Witness: Yes, your Honor; it is considered a safe cap.

The Court: Is it supposed to seal itself?

The Witness: Yes, your Honor; it is expected to be self- [185] sealing.

The Court: That is all I have.

Mr. Neukom: May I have one or two questions.

Q. This thiamine hydrochloride product, the one which has the 50 milligrams in it, what base is that in? Is that in an alkaline or an acid base?

A. The thiamine hydrochloride, when it is put in solution by itself, is very acid.

Q. Which is Government's Exhibit 2, the label?

A. Yes, sir.

Q. Well, that is a proper base to retain the efficacy of that vitamin product, is it not?

A. The acid base is the proper base,

Q. I would like to ask one thing on this cork, but not staying on it too long. When the hypodermic needle is placed in it, why, it seals, by the soft cork, all air from going in and merely allows the needle to go down, doesn't it?

A. It will stand to reason that it is impossible to take that vial and put a hypodermic needle in it and pull out a certain amount of solution, pull the hypodermic needle out,

(Testimony of Russell R. Bavouset)

and expect that to continue to form a vacuum. About the third time you place that hypodermic needle in there and pull it out, you will have a little trouble. The vacuum created inside that vial will cause a little difficulty in filling the plunger and it will be necessary to pull the plunger back and forth. It is common practice to place the [186] needle back in, pull out the air and let it run out.

Q. You buy your thiamine chloride in a bottle, don't you? A. Yes; or it comes in a powdered form.

Q. And that bottle has a screw cap on it, doesn't it?

A. Well, it comes in all different types. It is sealed up on the top and usually comes in carboys or drums.

Q. You do not always use all the product when you get it, do you?

A. We try to at once. That is, when you open a carboy that has been sealed up, we try to use the whole thing at one time.

The Court: Do you mean a 10-gallon jar?

The Witness: A carboy is like, we will say, just a container that contains usually one kilo, 1,000 grams.

Q. By Mr. Neukom: You did not use up a thousand grams when you made this product here that supposedly has the 500,000 units?

A. Working with Vitamin D there, sir.

Q. Oh, I beg your pardon. The one that had the thiamine chloride here.

The Court: 50 milligrams.

Q. By Mr. Neukom: 50 milligrams. You did not use up a whole can of it in compounding that allotment, did you? A. Yes; we generally do. [187]

(Testimony of Russell R. Bavouset)

Q. Well, you do not throw it away when you have some left, do you?

A. Not by any means. We usually compound a sufficient amount in a day to use up the entire amount at the time.

Q. But some sets around on your shelves, doesn't it?

A. A very short length of time.

Q. But it is your testimony these are rather a thick kind of rubber caps, aren't they; they are not just like a little sheet of rubber, are they?

A. That is particularly thick.

Q. They look like a quarter of an inch thick?

A. They are so thick they will seal off and keep air out even though a vacuum is formed inside.

Q. Do you mind if we take one of them?

A. I do not; no, sir.

Mr. Neukom: Do you, counsel?

Mr. Stick: I have no objection.

The Court: If there is a danger of air entering the bottle with treatment, intermittent use, that is, treatment with intermittent insertion of the hypodermic needle, should there not be some warning on the label that these properties such as thiamine hydrochloride are likely to become dissipated through entrance of air into the bottle over a period of time?

The Witness: It possibly would be a good suggestion, your Honor, to have a label stating that it should be used up [188] very rapidly after first puncturing.

The Court: In this product would it be harmful if it had twice as much as 50 milligrams of thiamine hydrochloride?

(Testimony of Russell R. Bavouset)

The Witness: No, your Honor. We have products, and there are many products on the market, that contain 100 milligrams of thiamine hydrochloride per cubic centimeter.

The Court: If you put more in than the label states, in order to be sure that at all times it has the labeled strength, there would be no harm could come from it?

The Witness: No, your Honor; there would not be.

Mr. Neukom: Your Honor may care to see what the cap is like. The plastic has been removed from it. There is a little paper adhering to the top of it.

The Court: The space intended for the insertion of the hypodermic needle is comparatively small in proportion to the surface of the cap, is it not?

The Witness: That is correct, your Honor; very small.

The Court: How many injections would this bottle hold, about?

The Witness: The average injection is about one cubic centimeter; so that would be approximately 30.

The Court: 30?

The Witness: Yes, your Honor.

The Court: How many times would you think a doctor could insert a hypodermic needle in the space provided here [189] in this cap before there would be a hole in it?

The Witness: Well, I have been given to understand it will go up to 100 times, though I have never tried it personally.

Q. By Mr. Neukom: At least, it should go more than the contents of the bottle? A. Yes, sir.

The Court: And is it your opinion that it will?

The Witness: Yes; it is, your Honor.

Mr. Neukom: That is all.

(Testimony of Russell R. Bavouset)

The Court: And unless there is some interference from the outside, presumably there would be no air enter the bottle to dissipate the thiamine hydrochloride?

The Witness: No, your Honor; there would not be.

Redirect Examination

By Mr. Stick:

Q. This type of cork or stopper is the common type in use in the industry for the handling of these kind of products? A. It is the common type.

Q. When you withdraw a cubic centimeter of liquid from a bottle, does that not create a vacuum to an extent?

A. That does create a certain vacuum; yes, sir.

Q. And when you withdraw another cubic centimeter [190] you would create still more vacuum?

A. Even more vacuum; yes, sir.

Q. After a while, if no air got in there, it would be difficult to withdraw?

A. It gets to the point where it cannot be withdrawn; that is right.

Q. Is it not a standard practice then, if you are going to withdraw a cubic centimeter of a material from a bottle corked as this, to pull the hypodermic syringe out to the one centimeter, cubic centimeter mark, then insert it into the bottle and then push your cap in, pull that much air in it and then hold it up so the air is at the top, and pull out your one cubic centimeter of the product?

A. That is true. It is the common practice to take the syringe, pull it back a certain distance, that is, the

(Testimony of Russell R. Bavouset)

plunger of the syringe, inject the air into it without creating a pressure in there, then merely turn it, for instance, down and letting the plunger be forced back to a certain part and pull it out for the injection.

Q. So that each time something was removed there would be air get into the bottle that had not been there at the time it was manufactured? A. That is true.

Q. Have you seen and been around medical offices while doctors were taking things from bottles of that kind? [191] A. Yes; many times.

Q. Is it a common practice to use more than one substance at a time in a hypodermic?

A. Very common.

Q. And when they do use more than one substance do they take the one substance out of one bottle and then continue the plunger back and let the air out from the extra part that is taken back and draw the substance in and mix them both in the same hypodermic?

A. Yes.

* * * * * * * * *

Mr. Neukom: Well, I would like to make this observation, if I may: It might save a little time. Your Honor, at this stage of the case there has been no evidence offered that the product examined by the experts had gone through any of these stages of repeated air going into them.

(Testimony of Russell R. Bavouset)

The Court: No. I probably led the case off onto that tangent. I was curious about this cork in the bottle.

Mr. Neukom: Very well.

The Court: I appreciate that the contention here is not based upon the supposition that something happened to the products in a doctor's office.

Mr. Neukom: Very well, your Honor. [192]

The Court: And, I take it with respect to the first six counts, at least, there is no issue as to whether the compound or liquid had any therapeutic value or not.

Mr. Neukom: We have no issue on that, purely the quantitative amount.

The Court: It is a question—

Mr. Neukom: Of whether the label says—

The Court: —of whether the product contains what the label says.

Mr. Neukom: That is the sole issue of the six counts.

The Court: And that is, as manufactured and as shipped.

Mr. Neukom: That is right, your Honor.

The Court: And specifically, as introduced into interstate commerce.

Mr. Neukom: That is right.

Mr. Stick: That is all. [193]

* * * * * * * * *

ROLAND N. ICKE,

called as a witness by defendants, being first sworn, was examined and testified as follows:

The Clerk: Please state your name.

The Witness: Roland N. Icke.

Direct Examination

By Mr. Stick:

Q. Dr. Icke, what is your occupation?

A. I am a director of research at the Pasadena Research Laboratories.

Q. Is your research in chemistry? A. Yes, sir.

Q. Any particular type of chemistry?

A. Organic chemistry, medicines, drugs.

Q. What is your educational background?

A. I received a Bachelor of Arts, a Master of Science, a Doctor of Philosophy degrees from the University of California at Los Angeles. I have had a year of medical training at the Medical School of the University of Southern California.

Q. Do you belong to any societies of the chemical [194] type?

A. Yes, sir. I belong to Alpha Chi, Sigma Alpha Epsilon, Alpha Kappa Kappa, Medical Fraternity, Sigma Chi national sorority, and American Scientific Affiliation, the American Medical Society.

Q. What experience have you had in research with reference to medical products particularly?

A. Aside from the research in connection with working toward my degrees in chemistry, I have had seven years of research in the pharmacology and chemistry laboratories of Dr. Gordon A. Alles in Pasadena. I have also had research experience at the Pasadena Research

(Testimony of Roland N. Icke)

Laboratories since February, 1946. I had one year of teaching experience as associate professor of chemistry and chairman of the department of chemistry at Westmont College.

Q. Are you familiar with the types of products that are in evidence here? A. Yes, sir.

Q. I will show you Government's Exhibits No. 6 and 7, No. 6 being a bottle or vial containing a solution, and the Exhibit 7 being a label from that, and upon that appears to be the words "PLURI-B". From that label or on that label appears the language "Thiamine Hydrochloride," I believe. A. Yes.

Q. That is commonly known as the B-1, Vitamin B-1? [195] A. Yes.

Q. Vitamin B-1, which actually is a food, isn't it?

A. Yes.

Q. Is that a stable product?

A. Under normal conditions it is.

Q. Under what conditions is it not a stable product?

A. Vitamin B-1 can be destroyed very rapidly if the solution is brought towards neutrality or on the alkaline side in a solution that must be kept acid in order to be stable. Also, it is susceptible to destruction by presence of sulfites, or it can be destroyed by oxidation, and in any of those cases that those agents were present which might cause destruction, any temperature above normal would speed the rate of destruction.

Q. You are familiar with the type of cork or bottle stopper that is used on these bottles that are in evidence?

A. Yes; I am.

(Testimony of Roland N. Icke)

Q. We have one bottle here open from which a cork has previously been removed. Have you made any test or examination to determine whether by visual examination with the eye, as you look at a bottle, you can tell whether that cork has been punctured or not?

A. Yes; I have tested that fact.

Q. What did you do and what was the result of that test? [196]

A. I took a bottle that had a fresh stopper on it, that I had reason to believe had never been punctured, and I looked at that under the microscope after first examining it superficially to determine if I could see with ordinary vision whether it had been punctured. Under the microscope I could not tell that anything unusual had happened to the stopper. It did not appear to have any hole in it.

Then, that stopper, I inserted a needle such as commonly used for hypodermic injections through that stopper, pulled it out and again looked at the stopper with my eyes and was not able to tell where the puncture had occurred. It had sealed, as nearly as I could tell, completely.

Then I took that same bottle, put it under a microscope and observed the top and, after a considerable difficulty, finally located the spot at which the puncture had occurred. There was evidence that a needle or some object had penetrated the cap.

The Court: Which bottle?

The Witness: The bottle which I tested experimentally in the laboratory to determine—

The Court: That was a new bottle?

The Witness: Yes.

The Court: It is not here?

(Testimony of Roland N. Icke)

The Witness: No. I feel, though, that that same thing would apply to any rubber cap, because I have looked at a [197] number of bottles which I have seen punctured with needles and, by looking at it just with the naked eye, you can't tell readily whether they have been punctured or not.

The Court: So you cannot tell by visual examination with the naked eye whether the corks in the two bottles comprising Exhibit 1 have been punctured?

The Witness: No; not unless there had been an extremely large needle used, and I am not even positive that I could then.

Q. By Mr. Stick: What will cause the oxidation of thiamine hydrochloride?

A. There are many oxidizing agents which are known to have an effect on thiamine hydrochloride. In the assay for thiamin, thiamin is subject to oxidation by potassium ferri-cyanide or some other material produced, thiachrome, which is an oxidation product, one of the inside products, at least, of thiamin.

There are other materials such as peroxides which, if introduced into a solution containing thiamin, might cause destruction.

Q. Are you familiar with the methods used by doctors in their offices? A. Yes, sir.

Q. In handling bottles, hypodermic syringes, etc.?

A. Yes. [198]

Q. Do doctors sterilize their syringes and needles before they take out doses of medicine from bottles of that kind?

A. It is the common practice to sterilize them; yes.

(Testimony of Roland N. Icke)

Q. And what things are used for that purpose?

A. Well, sometimes they use steam sterilization, or heating the things in boiling water. Others may use bichloride of mercury or various other bacteriacides. Also, it has become more and more common in recent years to use isopropyl solutions for sterilizing instruments.

Q. Before a bottle of that character is used for the purpose of withdrawing a dose of medicine is it customary to sterilize with some substance the cork before the needle is inserted?

A. Yes. The doctor usually takes a piece of cotton or gauze and wipes off the top of the cap with alcohol, isopropyl alcohol is often used.

Q. If any of that isopropyl alcohol was left in the needle and went into the bottle would it affect the content or the potency of the thiamine hydrochloride?

A. It might, because isopropyl alcohol is known to contain bacteriacides under many conditions. I have worked in a chemical laboratory at the time that discovery was made and observed the experimental work of the investigator, who showed that isopropyl alcohol often contained bacteriacides. [199] And I have also seen doctors taking solution to be injected from this bottle in which they have used isopropyl alcohol to sterilize their needle and syringe, and often, instead of drying the needle and syringe, they may just put the needle onto the syringe and move the plunger back and forth to pass a little air through it and get rid of most of the sterilizing agent. But I have seen them insert a needle into a bottle and which it was not completely dry, and because of their practice, introduce air into it. It would be possible for a

(Testimony of Roland N. Icke)

spray of a small amount of isopropyl alcohol, and, therefore, bacteriacide, to be introduced into that bottle.

Q. And would the amount that would be so introduced affect the thiamine hydrochloride in the bottle?

A. It would depend entirely on how much bacteriacide was in the isopropyl alcohol, how many injections had been withdrawn from the bottle, and how much bacteriacide was there just how much it would affect it. But even a small amount would affect it.

The Court: Immediately?

The Witness: The effect would start immediately; yes.

Q. By Mr. Stick: You have stated that air is injected into the bottle. Just what did you mean by that?

A. In order to prevent a vacuum in the bottle when withdrawing a needle, it is common practice to pull the [200] plunger of the syringe back to the mark at which you intend to take your solution, inject that equivalent amount of air into the bottle and then allow the pressure inside the bottle to aid in filling the syringe.

Q. Would that air have any effect on the thiamine hydrochloride?

A. Thiamin is susceptible to oxidation and air contains oxygen, so undoubtedly air would affect the stability.

Q. Do doctors at times use more than one substance in a hypodermic injection?

A. Yes; it is common practice.

Q. And in using that will you describe their method of getting the two substances or more substances into the syringe?

A. After their usual sterilization procedure, they will withdraw the plunger of the syringe back to the mark corresponding to the amount of the first solution they

(Testimony of Roland N. Icke)

intend to withdraw, and they will insert that needle into the cap and inject into that bottle that amount of air; then they will withdraw that solution into the syringe and withdraw the needle from the cap, and then will withdraw the needle or the plunger of the syringe farther back to correspond to the additional amount of material which they wish to take, then will insert that needle into the second bottle and inject the air in that bottle and then withdraw from the second bottle. [201]

Q. By that could any substance get into a bottle containing thiamine hydrochloride that might affect it?

A. It could very easily happen. Thiamine hydrochloride is only put up in acid solutions, pH. around 3.2 or thereabouts. There needs to be acid in order to maintain its stability. If a doctor chose to give an injection in which, for example, he was using sodium salt of Vitamin C or some other material which was more alkaline in nature than the B complex, if he withdrew this more alkaline solution first into his needle, into his syringe, and then injected air in intending to withdraw his second sample, if he injected some air into that second bottle, there would be some of the first solution remaining in the needle; so there would be a very good chance; in fact, it would be practically certain that some of the first solution would get into this bottle of the second solution.

Q. That could affect the potency of the thiamine hydrochloride?

A. That could affect the pH., affect the degree of acid.

(Testimony of Roland N. Icke)

Q. And if the acid is raised, the destruction of the potency would increase?

A. If the pH. is raised, the destruction rate would increase.

Mr. Stick: Your Honor, we have used in this case a [202] number of times the "pH." Are you familiar with what that is?

The Court: I am not sure whether I am or not.

Mr. Neukom: I am not.

Q. By Mr. Stick: Doctor, would you, below this diagram here, and with some chalk that we have—

Mr. Neukom: There is some right up there.

Q. By Mr. Stick: Would you draw a graph, illustrate what this pH. is supposed to be and how?

A. "pH." is a measure of the degree of acidity, the base acidity of a solution normally.

The Court: And it is a departure from neutrality, is that it?

The Witness: There is a specific pH. in water for neutrality. That pH. is 7. (Diagraming.) If I let this roughly represent the pH. scale, pH's. vary from one through 14, for example. Any pH. between 1 and 7 is acid, considered to be an acid solution. Any pH. above 7 is considered to be an alkaline solution; a pH. of 7 would be a neutral solution.

Vitamin B-1, if kept at a pH.—Vitamin B-1 solutions are kept at a pH. normally around 3.2, which is definitely acid, because it is stable at that pH. If that pH. is raised, though, by the injection of any alkali, then its stability is less.

The Court: As it trends toward an alkaline substance, [203] is it?

(Testimony of Roland N. Icke)

The Witness: Yes; as it becomes more alkaline it becomes less stable.

Q. By Mr. Stick: And as it becomes more alkaline does the rate of destruction increase?

A. Yes; considerably.

Q. Doctor, if you will look at the label of the exhibit you have before you, the bottle 6 and the label 7, you see on the label "riboflavin 1 mgm.", is that correct?

A. Yes.

Q. You see "Nicotinamide", is that it? Is that the correct pronunciation?

A. Is this 7? Yes. Yes; I see the word "Nicotinamide".

Q. And that is 50 milligrams? A. Yes.

Q. There is also—how do you pronounce this?

A. "Pontochenic acid, pyridoxine hydrochloride, riboflavin and thiamine hydrochloride," as well as the nicotinamide.

Q. You were here when the Government's chemist stated his method of analyzing the contents of Exhibit 6 for the purpose of determining the potency of the thiamine hydrochloride? A. Yes.

Q. Would you state that that test is a fair test in [204] the light of the other ingredients which are in that bottle?

A. It is generally considered as being reliable within certain limits of error.

Q. Would the nicotinamide have anything to do with the solubility of the riboflavin?

A. Very definitely.

(Testimony of Roland N. Icke)

Q. Will you describe what you mean and what action would take place?

A. Nicotinamide is known to increase the solubility of riboflavin. In fact, there are other ingredients also which make riboflavin more soluble than it would be in water alone; so that when you are dealing with a solution containing other things besides riboflavin and water, there really is no good measure of just what the solubility of riboflavin is in terms of its water-solubility, because water is no longer your solvent. You have a solution containing these other things which is your solvent. The solvent is not the pure water.

Q. Would the presence of the nicotinamide and, perhaps, the other substances increase the amount of riboflavin that could be dissolved into a product.?

A. Yes; very definitely.

Q. A definite amount of solution?

A. Yes. I have seen products on the market which contain as much as five and three-tenths milligrams of riboflavin per cc, when other ingredients in those were present, [205] and have in my possession a sample purchased on the open market which contains four milligrams per cc of riboflavin.

The Court: A clear liquid?

Q. By Mr. Stick: And does that also contain thiamine hydrochloride?

A. I believe so. It contains 10 milligrams of thiamine hydrochloride, four milligrams of riboflavin, and 20 milligrams of niacinamide per cc.

The Court: Does it contain any nicotinamide?

The Witness: Yes, sir.

(Testimony of Roland N. Icke)

The Court: Is it a clear solution, without precipitation?

The Witness: It has some precipitation. It is very difficult to detect. The amount is considerably—is a very small amount.

Q. By Mr. Stick: Would you say that the formula set forth on the label, Exhibit 7, which was on the exhibit bottle, No. 6, contains an undue or unreasonable amount of riboflavin in the light of the other ingredients that are contained in the solution? A. No.

Q. Are you familiar with the general practice of doctors in the handling of their medicines and so forth in their offices? A. To a certain extent; yes.

Q. You have been in medical offices? [206]

A. Yes; many of them.

* * * * * * * * *

Q. Is it customary when one of these bottle like we have here, containing, say, 30 cubic centimeters of a product, when it has been used, say, once or twice to throw it away?

A. No. The doctor puts it on his shelf, ready for [207] use next time.

Q. Do they ever diliberately insert other things into bottles to make a different combination of a product?

Mr. Neukom: Your Honor, I will stipulate that they do.

Mr. Stick: All right; that is all I asked for.

The Court: Very well.

Q. By Mr. Stick: Turning to Exhibit Nos. 3 and 4—your Honor, while we are on this same subject of the Pluri-B, I will withdraw this 3 and 4 and show the wit-

(Testimony of Roland N. Icke)

ness Nos. 1 and 2, because it is substantially the same product and the testimony would be more or less along the same line, I would imagine.

Will you examine those bottles as to their content? What do you observe by examining the bottles?

A. There is a precipitate in it.

Q. I will ask you to examine the labels on Exhibit No. 2 and you will find there, I believe, riboflavin 2 milligrams, is that correct? A. That is correct.

Q. What other products are in that solution besides the riboflavin?

A. This solution also contains 50 milligrams of the thiamine hydrochloride, 10 milligrams of pyridoxine hydrochloride, 10 milligrams of pantothenic acid, and 50 milligrams of nicotinamide. [208]

Q. Now. save for the riboflavin, the ingredients and the amounts of the ingredients as shown on Exhibit 2 are the same as shown in Exhibit 7 which you had before you a few moments ago?

A. I believe that is correct.

Q. The riboflavin, however, has one milligram more than it did in the Pluri-B which you have been testifying to heretofore under Exhibits 2 and 3, I believe?

* * * * * * * * *

The Court: Exhibit 6, the label to Exhibit 6 is Exhibit 7, which contains one milligram of riboflavin; and the Exhibit 1—

Mr. Stick: Now he has 1 and 2 before him.

The Court: Yes. They contain two milligrams, as I understand it, is that correct?

The Witness: That is correct.

(Testimony of Roland N. Icke)

Q. By Mr. Stick: And other than that, they are apparently the same, is that correct? A. Yes.

Q. Now, would you say that in the light of the substances contained in the bottles before you, Exhibits 1 and the label 2, that the two milligrams of riboflavin was an excessive amount?

A. No; I would not. [209]

Q. Did you hear Dr. Wiley's testimony with reference to that? A. Yes.

Q. I believe that he made the statement that that was a supersaturated solution of riboflavin?

A. Yes.

Q. Would you call that a supersaturated solution of riboflavin? A. No; I would not.

Q. Will you state why?

A. Because I have seen other products containing more than that much riboflavin which did not have a precipitate in it; and also, because I have seen products containing less which did have a precipitate in it; so it is apparent to me that some other factor must be involved.

Q. In examining the bottles in Exhibit 1 and observing the precipitate that you find therein, would you be able to state when that precipitate occurred in that bottle? A. Certainly not.

Q. Could you say whether the precipitation took place within, say, a week of June 18, 1946?

A. It would be impossible to say, without exact knowledge, just when that precipitation did occur. I have made up solutions of Vitamin B complex, trying to solve the precipitation problem and some of the experimental solutions [210] I made up I was feeling pretty good about

(Testimony of Roland N. Icke)

it, thinking that the problem had been solved. They stood in solution for sometime and then, on coming to work the next day, there was a precipitate in it. If I had not known the history of that in the meantime, I could not have said when that precipitation occurred.

The Court: What do you mean by "for some time?"

The Witness: A period of three or four days or a week.

The Court: Did you keep it in closed bottles?

The Witness: Yes.

Q. By Mr. Stick: Those experiments contained heavy doses of it? A. Yes.

Q. Is riboflavin itself soluble in water?

A. Very slightly.

Q. What are the bases in which it is dissolved?

A. I believe it has some solubility in alcohol, but I know that the presence of some other ingredients in a water solution will increase its solubility.

Q. Such as you have testified to? A. Yes.

Q. And in order to increase its solubility, some of these other substances are introduced? A. Yes.

Q. What factors affect the time in which a substance [211] of this type of solution will precipitate?

A. That is very difficult to say.

Q. Are there factors which could affect the precipitation such as you have in the bottles in Exhibit 1 after they were manufactured?

A. If the doctor had used any of that material and had carried out one of these injections where he had first used another material, so that he was mixing the two things, and had introduced some of the other material in here, by that he could have changed the nature of the

(Testimony of Roland N. Icke)

solvent, the material could have changed the nature of the solvent in which the riboflavin would dissolve.

Q. Under those conditions of temperature at which it was kept, would that affect the break-down of the substance or the precipitation?

A. It might, particularly if he had introduced any oxidizing materials or any substance which would increase the alkalinity.

Q. Have you made any tests of solutions similar to this which contained undissolved particles of pyrogen?

A. Yes. I tested a similar preparation containing undissolved particles injected into rabbits, and observed that their body temperature was not raised.

Q. Just describe to the court what you mean by pyrogen? [212]

A. The pyrogen test is prescribed by the U. S. P. as a means of determining whether or not a product is safe for injection.

Q. "Pyrogen" means what?

A. "Pyrogen" refers to the raising of the body temperature.

Q. Ordinarily spoken of as— A. Fever.

Q. —fever. All right. Then after you made this pyrogen test of this substance containing undissolved particles on the rabbits did you carry the experiment any farther?

A. Yes. I withdrew in a needle and a syringe some of the solution, observed it, and saw that there were particles suspended in the solution in the syringe, injected it into my own arm and observed no ill effects whatsoever.

(Testimony of Roland N. Icke)

The Court: This was a precipitate of riboflavin?

The Witness: Presumably it was riboflavin. That is the material which is generally considered as being what precipitates in all of these B complex solutions.

Mr. Stick: Might I have this bottle that has been referred to by the doctor as containing four milligrams of riboflavin—may I have that marked for identification?

The Court: You may.

The Clerk: Do you want the box marked, too?

Mr. Stick: What? [213]

The Clerk: Do you want the box also marked?

Mr. Stick: I don't think that will be necessary; just the bottle.

The Clerk: This will be B for identification, Defendants'.

Q. By Mr. Stick: This product in the bottle marked Exhibit B, is that of the same general character as the things contained in Exhibits 1 and 2?

Mr. Neukom: Well, I don't like to object, but I think that is a matter the court ought to decide. It is obvious from my interpretation of the amounts there that it is not compounded similarly in amounts.

The Court: Overruled. He may answer.

A. That is also a Vitamin B complex preparation, as this says.

Q. By Mr. Stick: I believe you testified that it has some precipitate in it? A. Yes.

Q. Have you examined other similar Vitamin B products on the market as to whether or not they contain precipitates?

A. Yes. I purchased from Horton and Converse, and also from the Exclusive Prescription Pharmacy sev-

(Testimony of Roland N. Icke)

eral B Complex preparations put out by first-line pharmaceutical houses. I merely asked for a B Complex preparation and accepted whatever product they gave me.

Q. And that was true when you got Exhibit B? [214]

A. Yes.

Q. And did these preparations have precipitate in them? A. They did.

Q. And how much riboflavin was in these different bottles that you bought?

A. Well, varying amounts. I have one here that had only a half a milligram of riboflavin and it has precipitate in it.

The Court: Let that be marked for identification.

Mr. Stick: Yes, sir.

The Clerk: C for identification.

The Court: The bottle with the label on it?

The Clerk: Yes. The label says "Vitamin B Complex Parenteral 10 cc."

The Court: What was the riboflavin content?

The Witness: One-half milligram per cc.

Q. By Mr. Stick: You have shown one additional bottle, is that it? A. Yes.

Q. Is that the only other one you had?

A. No. I have others that I purchased at the same time.

Q. Do they contain precipitates?

A. Yes; they do. [215]

Q. They are B-1 solutions?

A. They are B Complex.

Q. B Complex solutions? A. Yes.

The Court: Do you wish them marked, Mr. Stick?

(Testimony of Roland N. Icke)

Mr. Stick: I think it would be well if they were. Will you describe each one of them and hand them to the clerk one at a time so that the clerk can mark them?

The Witness: This solution is called "VIJEX", V-i-j-e-x, produced by Galen Company, Inc., in Berkeley, contains per cc 10 milligrams of thiamine hydrochloride, ½ milligram of riboflavin, 10 milligrams of niacin amide, 10 milligram of pyridoxine, 10 milligrams of pantothenic acid.

Mr. Stick: May that be marked D?

The Clerk: D for identification.

The Court: Do you have another one?

The Witness: Yes, sir.

The Court: The witness might describe it.

Mr. Stick: All right. Will you describe it?

The Witness: This is a product put out by Parke, Davis and Company. It says "Vitamin B Complex Parenteral."

Q. What does that mean?

A. It means that it can be injected. "Each cc. contains: Vitamin B_1 10 milligrams, Vitamin B_2, or riboflavin, 2 milligrams, Vitamin B_6, or pyridoxine hydrochloride, 5 milligrams, nicotinamide, or niacinamide, 50 milligrams, [216] pantothenic acid (as the sodium salt) 10 milligrams." These substances also contain preservatives.

Q. Does this substance contain a precipitate?

A. I believe it does, a small amount.

The Court: Let that bottle be marked.

The Clerk: E for identification.

(Testimony of Roland N. Icke)

Q. By Mr. Stick: Now, in those bottles which you have introduced and said that you purchased at the pharmacy or pharmacies in the open market, and which contained the B-1 or B Complex solutions, and which you said had to some greater or less degree precipitate, can you tell from the examination of either of those when that precipitation occurred? A. Absolutely not.

Q. Did you ever make any test to determine whether that will go back into solution in any of these products?

A. Yes; on some materials I have tested and found that by warming them slightly the precipitate goes back into solution.

Q. That is in these B Complex? A. Yes.

Q. By the words "warming slightly" what would you mean?

A. Elevating the temperature above room temperature, but not up to boiling or anything like that.

Q. By how much would you say you would increase it over the amount that it had at the time that you started the [217] experimentation?

A. Probably would raise the temperature up to 50 or 60 degrees Centigrade.

Q. Which would be how much Fahrenheit?

A. That would be approximately in the range between 110 or 125 degrees Fahrenheit.

Q. And in some of those products which you have experimented with the matter would go back into solution from the precipitate? A. Yes.

The Court: In your opinion, would the precipitate in the two bottles comprising Exhibit 1, if they were placed in a pan of hot water?

(Testimony of Roland N. Icke)

The Witness: I believe it would. I would have to try it to be sure.

* * * * * * * * *

Q. You have before you now Exhibit 3, which is a bottle, and Exhibit 4, which is the label from that bottle, the label having on it the word "Indoform". Are you familiar [218] with that product?

A. Yes; I am.

Q. You see on that label the words "Thyroid Substance" 1 grain? A. Yes.

Q. Will you describe what would be meant by thyroid substance? A. With reference to this solution?

Q. Well, generally, and then with reference to that solution.

A. Thyroid substance, generally, or thyroid would refer probably to or would refer to dessicated thyroid powder which is generally given by mouth for treatment. An aqueous extract of thyroid substance would merely refer to that material which would be dissolved by water from the dessicated thyroid gland.

Q. Is there anything on that label which would indicate to a doctor whether that is a water-solution or extraction?

A. The very nature of the product itself, the fact that it is a glandular extract, would indicate to him that it is a water-solution.

Q. Would he, looking at that label, expect to find, normally, thyroxin in the solution?

A. Certainly not. [219]

(Testimony of Roland N. Icke)

Q. Why?

A. Because a doctor, if he wants thyroid activity, knows that for treatment he will give thyroid orally, that is by mouth. If he wants thyroid activity, he does not use an aqueous extract to obtain thyroxin, because thyroxin is not soluble in water. A great point of that is made in biochemistry, which every doctor is required to take, that the thyroid activity is almost unique in glandular hormone products, in that it is active by mouth. Many gland products are active only by injection, but thyroid is unique in being active by mouth; and that point is emphasized in biochemistry which every doctor takes.

Q. If there were no thyroxin—that is the part of the thyroid which contains the iodine—present would there be in an aqueous solution such as this a thyroid substance present? A. Yes; there would be.

Q. And that is the substance that is referred to in the label? A. Yes.

Q. Could you describe that substance?

A. To the best of my knowledge, there is no known chemical itself whereby it can be detected. I do know, though, that if thyroid substance or dessicated thyroid is extracted with water and the solution filtered so that you have a clear solution, that when that solution has evaporated there is a [220] residue, therefore, there is something dissolved.

Q. Would the Elmslee-Caldwell test for iodine disclose those substances which are in the aqueous solution?

A. That test is for organically combined iodine, and there is a test for thyroxin or other iodine-containing compounds characteristic of the thyroid gland. Since

(Testimony of Roland N. Icke)

this solution does not contain any thyroxin, you would expect to get a negative result. There would be no point in even assaying it for iodine.

Q. You will notice "posterior pituitary" is referred to on that label? A. Yes.

Q. Three international units. How is that extracted and put into that solution?

A. I have never extracted it myself. It is my understanding that it is also an aqueous extract. It certainly must be, in the fact that it appears in this aqueous solution.

Q. Are there any substances which will affect the thyroid substance that you have described, in the sense that it will destroy either the potency of the posterior pituitary or the thyroid substance? [221]

* * * * * * * * *

A. I do not know of anything definitely in thyroid substance, as such, which might cause destruction of the posterior pituitary; but there are other ingredients in this same solution which might.

Q. By Mr. Stick: All right. What, for instance?

A. The suprarenal cortex, 30 grains. Suprarenal cortex extract, as prepared, almost invariably—I would say invariably—contains adrenalin or epinephrin; so that in a mixture of suprarenal cortex and posterior pituitary the mere presence of any adrenalin, although in this dose it would not be harmful to the human body, would repress any tests which were designed to show the presence of posterior pituitary. Adrenalin is an antagonist to a test as described by Mr. Mason.

(Testimony of Roland N. Icke)

The Court: What is this other substance you mentioned besides the adrenalin?

The Witness: Adrenalin was the one that I was referring [222] to.

The Court: Earlier, you say, "adrenalin" or some other substance.

The Witness: I know that from—

The Court: That it might contain.

The Witness: I know from experience.

The Court: No. I am just asking you that.

The Witness: Inherent.

The Court: You said that, due to this suprarenal cortex, that that substance might contain two substances, adrenalin and something else; and I did not understand the other substance.

The Witness: Adrenalin or epinephrin. "Adrenalin" is synonomous with "epinephrin".

The Court: And what is epinephrin?

The Witness: It is another name for the same thing.

The Court: For adrenalin?

The Witness: Yes.

Q. By Mr. Stick: Is adrenalin common in suprarenal cortex? A. Yes; it is.

Q. I understand, then, that what you mean is that the presence of suprarenal cortex in this solution would inhibit a test for or would interfere with the correct test for posterior pituitary as described by Mr. Mason? [223]

A. That is true.

Q. And would it show lesser or greater activity?

A. Since the effect of adrenalin is antagonistic or inhibitory to posterior pituitary, and posterior pituitary that was there would not be allowed to show its presence.

(Testimony of Roland N. Icke)

Q. So that the posterior pituitary under the circumstances would not, under that test, be as active as it would if the adrenalin was not present?

A. No; it would not. [224]

* * * * * * * * *

Mr. Stick: That is all.

Cross Examination

By Mr. Neukom:

Q. Dr. Icke? A. That is right.

Q. Doctor, there would be quite a dilemma if your theory is correct in the use of these items, wouldn't there? If he uses the alcohol or any sterilizing agent, he is going to ruin the efficacy of the product and take that chance?

A. Yes.

Q. If he does not use them, he is going to take a chance in giving his patient blood poisoning or some other infection, isn't he?

A. He could use some other sterilizing means or be careful that his syringes and needles were dry.

Q. When you made this product—well, incidentally, [227] right on that point, none of those four products here you had anything to do with their compounding, did you? A. No.

Q. The ones that are here in evidence, charged in this case? A. No.

Q. But you knew, and it is common knowledge, when these products were made that doctors did follow those means of sterilizing their needles, didn't they?

A. That had not been drawn to my attention until I had occasion to observe a bottle in which precipitation had occurred and that factor occurred as a possibility.

(Testimony of Roland N. Icke)

Q. Now, Dr. Icke, let us look at this Squibb product here, which is Defendants' B. And the bottle here, it is known as Parentosol. As a matter of fact the precipitation in that is so minuscule that you can hardly see it, isn't that true? A. It is hard to see.

Q. And let us look at the product that was put out by your employer, and the particles in there are large, some of them are?

A. Those could be very readily seen.

Q. The ones in the Exhibit B you can hardly see; isn't that true? [228]

* * * * * * * * *

A. Yes.

Q. This Exhibit 2 goes with Exhibit 1, the vial from Exhibit 1. Let's you and I compare the two component parts here, thiamine hydrochloride, from Exhibit 2; that label is 50 milligrams per cubic centimeter; isn't that right? A. That is right.

Q. Let us look here on Exhibit B; thiamine hydrochloride is only 10 milligrams; isn't that right?

A. That is right.

Q. All right. Riboflavin is 4 mgms. on the Squibb product, Exhibit B? A. Yes, sir.

Q. And it is 2 on your product?

A. That is correct.

Q. Now, nicotinamide. A. Niacinamide.

Q. Niacinamide, which you state helps dissolve the riboflavin; isn't that correct?

A. It is one of the things that helps.

Q. That is the same material as on Exhibit 2 called "nicotinamide"? A. Nicotinamide.

(Testimony of Roland N. Icke)

Q. Spelled a little differently here, but it is the same product, isn't it? [229]

A. There are two names that are used: Niacinamide or nicotinamide. They are the same.

* * * * * * * * *

Q. And these two names are here from Exhibits B and 2? A. Yes, sir.

Q. Let us notice the great difference. There are 200 milligrams to four milligrams of riboflavin, whereas in your product there are only 50 milligrams to 2; or, in other words, it is four times as much, isn't it?

* * * * * * * * *

A. That is true.

Q. And you state that that nicotinamide has a tendency to dissolve the riboflavin?

A. It assists the solution; yes.

Q. It assists. Then, in your opinion, this is a better combination, if you expect to have undissolved particles, isn't it?

A. Not necessarily, because of the other substances also in solution.

Q. Would you, Doctor, be surprised if it were true that this Government's Exhibit 1, one of these vials, has [230] been placed in a very warm, almost boiling, bowl of water and still these particles did not dissolve?

A. I would expect them to dissolve.

Q. Doctor, have you noticed on Exhibit B that you brought here, in which we can virtually see if there are any particles there, do you note that it says right on here with the package: "If crystals of riboflavin form,

(Testimony of Roland N. Icke)

they may be dissolved by immersing the vial in lukewarm water."? A. Yes.

Q. Do you note anything like that on Government's Exhibit 2? A. No.

The Court: You are referring to the box which contains Exhibit B for identification?

Mr. Neukom: Yes, your Honor.

* * * * * * * * *

The Court: Is there objection, Mr. Stick, to marking the box in which it came a part of Exhibit B for identification?

Mr. Stick: No, your Honor.

Mr. Neukom: Incidentally, may it be so marked?

I note the Squibb bottle has, in addition to the rubber stopper that you can see, there is a metal stopper, too? [231] A. Yes.

Q. Which has to be taken off before it can be utilized, is that correct? A. That is correct.

Q. That has been on the market for some time, hasn't it? A. I have seen it on several products.

Q. However, the trade has found that these rubber caps in the fashion that your firm uses and other firms use is quite acceptable, haven't they? A. Yes.

Q. And, as a matter of fact, Doctor, this testimony that you have given with respect to doctors introducing, for instance, with the Vitamin B material, the thiamine hydrochloride, introducing some oxidizing agent, or as a result from this alcohol that you mention, or from the mercury substance or any of these other sterilizing agents, that is upon the assumption, is it not, Doctor, that that

(Testimony of Roland N. Icke)

has actually been introduced into the vial and has caused a deterioration; isn't that true? A. Yes.

Q. And had not such an agent been introduced, and if it be true that no air had gotten in, why, you would not expect any deterioration in any of these products containing either the Vitamin D or the Vitamin B-1, the thiamine [232] chloride, would you?

A. If it had been kept under normal conditions, I would not.

Q. What would you assume to be above normal conditions on B-1 as far as temperatures are concerned?

A. That would be a relative matter.

Q. Well, what would be in your opinion above?

A. I would say that any temperature above 100 to 120 degrees Fahrenheit might be above what you would consider normal.

Q. If the bottle was sealed as in that bottle, would you expect it to deteriorate within a matter of a few months down to only 33½ per cent?

A. If that bottle had been setting in the sunlight so that the temperature got up high, or any other factor which might have elevated the temperature, it might have deteriorated.

Q. Let us assume that the bottle had been kept in normal temperature. It has been your practice and observation of most doctors that they try to keep their bottles in proper places, has it not, Doctor?

A. I believe most of them do; yes.

Q. And it is rare that you find a doctor but what he adheres to the cautions that he has been instructed; isn't that correct? [233] A. Yes.

(Testimony of Roland N. Icke)

Q. You would assume, would you not, Doctor, that had this bottle not been opened and another agency placed into it that would have caused its deterioration that you speak of, that you should expect, in three or four months or even longer, that that substance would remain stable, wouldn't you? A. Yes.

Q. You would be rather surprised to find it was short about 30 per cent, would you not, or 33 1-3 per cent?

A. Yes.

* * * * * * * * *

Q. By Mr. Neukom: Doctor, what is there on this label here, this Indoform label, that shows that this is an aqueous solution?

A. The fact that it is an extract of glands.

Q. I am referring to Government's Exhibit 4, the first count. Now, do you not put up extracts of glands in a soluble solution and in an aqueous solution and expect some therapeutic value from it?

A. Some glands; yes. [234]

Q. Well, wouldn't you put up a thyroid substance in that manner and expect any therapeutic value?

A. Certainly not.

Q. Then, in other words, when thyroid is placed in a solution it has no value of a therapeutic nature whatsoever?

A. It has no thyroid activity that is known. That does not mean that it does not have any value.

Q. Well, what do you mean by that?

A. I mean that if a doctor wanted to use a product for the thyroid value, he would give thyroids in a solid form by mouth. He would not—

(Testimony of Roland N. Icke)

Q. Doctor, haven't you heard of many, many people taking injections of glandular substances containing thyroid by intravenuous or intramuscular?

A. They are for other conditions besides thyroid disorders normally.

Q. What are they for?

A. I am not familiar with the exact use, but I do know that if a doctor wants thyroid—the benefit of thyroid, he gives it by mouth and not by injection.

Q. But you will concede, Doctor, that you know that there are solutions given intravenously or intramuscularly of thyroid substances which are taken for a specific purpose, is that right? [235] A. I don't know how—

The Court: Do you mean by that, for the purpose of thyroid relief?

Mr. Neukom: Yes; some therapeutic value from thyroid.

A. Not for the therapeutic value of thyroid, I would not say.

Q. Aren't there extracts of glands, thyroid glands, which are made up in water solvents? A. Yes.

Q. Do you know of any other thing in which they dissolve thyroid substance into? A. No.

Q. Do they dissolve it into alcohol?

A. I don't know. An alcohol solution probably would not be injectable.

Q. Do you know of any published work or anything that you have read, Doctor, which indicates that a water-soluble extract of thyroid has any physiological effect?

A. No.

(Testimony of Roland N. Icke)

Q. Are we to understand that this, then, this product here, the thyroid substance, was a nullity; it really meant nothing?

A. To the best of my knowledge, there is no therapeutic value from an aqueous extract of thyroid substance.

Q. Doctor, you have stated that this adrenalin that [236] was present in this—I can't remember these terms.

The Court: Suprarenal cortex.

Q. By Mr. Neukom: —suprarenal cortex has a tendency to make it impossible, or it sort of works against the discerning of the presence of posterior pituitary, is thart correct? A. That is correct.

Q. Do you mean by that that it makes the posterior pituitary less efficacious? I am referring now to Government's Exhibit 4.

A. No; I don't mean that it makes it less efficacious.

Q. Well, do you mean that the analysts can't find and could not hope to find posterior pituitary because of its presence?

A. It would depend upon the relative amounts of adrenalin and posterior pituitary whether you could detect the presence of either one of them in the test.

Q. Oh. In other words, there isn't any assurance here as to the amount, then, of adrenalin that is present in Government's Exhibit 4?

A. I know of no assay to determine quantitatively that amount that is present there in that sample.

Q. Well, then, you just assume that this suprarenal cortex does contain adrenalin which might be enough to make you unable to determine whether or not there was

(Testimony of Roland N. Icke)

posterior [237] pituitary present in the amounts as indicated on that label?

A. I have assayed solutions which were made by extraction of suprarenal cortex and other glandular materials and have found adrenalin present.

Q. Well, let us take this one right here; that is the one we are interested in. Would you say that the suprarenal cortex of 30 grains per each cubic centimeter—is it your testimony that that is a sufficient amount and contains a sufficient amount of adrenalin that you can't hope to find posterior pituitary when you analyze that and follow the tests that have been testified to here by Mr. Mason?

A. I would have to analyze it for the adrenalin in order to be able to answer that question.

Q. Well, in other words, you were just surmising when you said that a while ago; you have no specific knowledge on whether or not that suprarenal cortex does contain an amount sufficient to eradicate the hope to discover the posterior pituitary?

A. I know that it takes only a small amount of adrenalin to counteract the effect.

Q. Vedy well. Take Defendants' Exhibit No. D, the Vijex product and, Doctor, make a fair comparison of that product with a portion of vial No. 1, from the vial, Exhibit No. 1; isn't it true that the fragments, if any, in D are almost undiscernable? [238]

A. Yes; they are hard to see. [239]

* * * * * * * * *

Mr. Stick: I would like to ask that the exhibits we introduced for identification yesterday—I believe it is B, C, D, and E—be now admitted into evidence.

(Testimony of Roland N. Icke)

Mr. Neukom: No objection.

* * * * * * * * *

The Court: Defendant's Exhibits for identification A, B, C, D, and E are now received into evidence.

* * * * * * * * *

By Mr. Neukom:

Q. Dr. Icke, I was inquiring of you with respect to what is the subject matter of Count VII, the undissolved particles in the vial, a part of Government's Exhibit No. 1; [241] and you had produced certain other vials such as B, C, and D, the products, and we had discussed them, asked questions and answers had been given with regard to those. I believe it was your statement that, in your opinion, these undissolved particles should dissolve in warm water or in lukewarm water, is that correct?

A. I would assume that they would.

Q. Would that be in water, say, around about 110-120 degrees Fahrenheit? A. I would guess so.

Q. Well, is that your opinion? A. Yes.

Q. Then, if Government Exhibit No. 1, the vial, does contain undissolved particles of riboflavin, that is the Pluri-B—no; it is the Pluri-B product which had two milligrams in it—it is your view that the riboflavin was not fully dissolved, is that correct?

A. I didn't say that.

Q. Well, then what is correct on that?

A. You are referring to the exhibit?

Q. I am referring to Exhibit 1, the vial, and then the label, which is Government's Exhibit 2, the Pluri-B

(Testimony of Roland N. Icke)

which had two milligrams, whereas the other Pluri-B had one milligram.

A. It is my opinion that something has happened to [242] the solution so that the riboflavin is no longer dissolved.

Q. I see. Doctor, do you know how that solution is prepared? A. In a general way.

Q. Just explain.

A. I know that the different ingredients are dissolved in water. This particular solution I am not certain the order in which the ingredients are dissolved. I know that they are finally all in the same solution and are disolved by warming.

Q. Well, they are all put into one glass basin and mixed, and then ultimately put into a large bottle—or would that be the correct procedure—and then, later, drawn off into the individual vials?

A. That would be the general idea.

Q. I see. When we have a condition of precipitation such as in Government's Exhibit No. 1, we have what is called supersaturated solution, do we not, of the riboflavin?

A. In the present condition of this bottle, I would say that that probably is correct.

Q. Well, if it was fully saturated, it would be dissolved; that would be correct, wouldn't it? When anything is supersaturated in the tenor of your terms, it is because the aqueous solution or the solvent is not able to dissolve the particles; isn't that correct? [243]

A. That is correct with reference to the particular condition of the solution at the time when that condition exists.

(Testimony of Roland N. Icke)

Q. I see. Now, Doctor, is it not your opinion that if this product was made and left to stand a period of time of overnight, and it had too much riboflavin in it, that within a short period of time that would show up, wouldn't it? A. Yes.

Q. And if a person was being careful and cautious when preparing the sterile solution such as this for intravenous or intramuscular use, they should, by experimentation, seek to ascertain when the other solvents or water or medicaments are ample to dissolve the riboflavin, shouldn't they?

A. Yes; that is the purpose of inspection.

Q. And that would not be very difficult, would it?

A. No.

Q. And if a manufacturer would but wait a short while and allow his solution to stand, he would readily detect that this condition was existing and could correct it, could he not? A. I believe so.

Q. Now, Doctor, yesterday we were discussing your views with regard to the possible existence of adrenalin in the suprarenal cortex of the solution known as Indoform, which is Government's Exhibit No. 4, the label is. Will you [244] please tell the court what gland the adrenalin gland is and where it is located?

A. The label on the bottle speaks of "suprarenal cortex extract", as I remember.

Q. Suprarenal cortex 30 grains, I believe, in each.

A. The suprarenal gland is also called the adrenal gland and is located near the kidney, generally.

(Testimony of Roland N. Icke)

Q. The adrenal gland and the suprarenal gland are the same?

A. The adrenal and the suprarenal, they are two names for the same gland.

Q. For the same gland. Do you know what term or word the "adrenal" comes from?

A. It would only be by surmise. It is my understanding that the word "renal" refers to kidney, and "adrenal" would be near the kidney.

Q. The gland, is it not divided up into two parts?

A. That is true.

Q. And what are the two parts?

A. The cortex and the medulla.

Q. And the medulla is the part of the gland from which the adrenalin comes; isn't that correct?

A. It originates in the medulla.

Q. And the cortex itself is not the gland which contains that substance, is that right? [245]

A. It is impossible to remove all of the medullary substance from the cortex; so that suprarenal cortex always contains some of the medulla and, therefore, always contains adrenalin.

Q. Now, you were here when Mr. Bavouset testified as to how he prepared the Indoform in question here. As I recall he stated that, with regard to the thyroid substance in this product reflected by Government's Exhibit No. 4, he mixed them up in a water solution and shook it to some extent; in fact, I think he said a day elapsed before he mixed it with the other products; isn't that correct, or do you have a recollection of that?

A. I do not recall exactly.

(Testimony of Roland N. Icke)

Q. Well, do you know if that is the way it was prepared?

A. I don't know the time intervals. I have never made any of the combination.

Q. Are you acquainted with how the suprarenal cortex is dissolved or is added to this compound?

A. Only that it is dissolved in water; I know that.

Q. And is it not, of course, exposed to air and to oxidation in so doing?

A. The extracts that I have seen made have been in bottles that were stoppered.

Q. In the process of packing it, of course, it is [246] exposed to the air, is it not? A. To some extent.

Q. And is it not true that the very small amount of adrenalin that might be in the suprarenal cortex, if the suprarenal cortex substance is pure, as established by the United States Pharmacopoeia, is rapidly deteriorated by air and oxidation?

A. It is my understanding that the Pharmacopoeia states that there is a certain percentage of adrenalin in U. S. P. suprarenal cortex. That is my recollection. And I know that on assays of finished preparations of this type I have found adrenalin in solution.

Q. Haven't you also found that adrenalin also acts as a contracting agent as applied to the uterus, or have you ever performed the test?

A. I do not recall that fact.

Q. You do not know whether it does, then, or it does not?

A. I know that in general, as far as I know it,—well, I would say practically always, as far as I know,

(Testimony of Roland N. Icke)

it always causes a relaxation on smooth muscles which are used for testing its activity.

Q. Doesn't it also contract muscles?

A. I don't know.

Q. You don't know. Well, what makes you say that [247] adrenalin negatives the effect of posterior pituitary?

A. Because posterior pituitary will contract smooth muscle and adrenalin will relax smooth muscle; so that there is an antagonistic effect.

Q. That is true if you have adrenalin in some large amount, rather than in the amount which is very insignificant in a pure product of suprarenal cortex; isn't that true?

A. I have a reprint, if I may draw it to your attention, in which only one millionth of the mol of adrenalin causes a relaxation of small muscle.

Q. Do you wish to refer to either one of these books?

A. All right.

Q. Your counsel has handed me these, and I don't know where.

A. On pages 137, 138, and 139 of this reprint I have circled some micrograph tracings showing the effect of a tenth of a minus six molal of epinephrin, 10 to the minus 6 meaning one-millionth of a mol.

Q. Does this test also embody the usage of posterior pituitary? A. It does not.

Q. Well, that is adrenalin, then, of itself, isn't that right? A. Yes.

Q. Have you ever performed a test on a uterus en- [248] deavoring to ascertain whether or not posterior pituitary in combination with a pure substance of

(Testimony of Roland N. Icke)

~~(cerebral)~~
suprarenal cortex would retard or restrict a test such as Mr. Mason testified to here?

* * * * * * * * *

A. Not on posterior pituitary itself, I haven't; but I have observed a test on other agents which also cause contraction of the smooth muscle and have observed the inhibiting effect of adrenalin on the contraction. And I know that the presence of adrenalin in combination with a material which, by itself, would cause contraction inhibits that contraction so that you will not get the full extent of the contraction which this other substance, by itself, would show.

It is my opinion that I have graph 1-B in which pure posterior pituitary in water and diluted acetic acid, as Mr. Mason described it was tested, that if he had also put some adrenalin with that, he would have got a smaller con- [249] traction; that curve would not be extended as high and, with proper amounts of epinaphrin, he might have gotten no contraction at all, and with further amounts, he might even have received an acute relaxation.

Q. How much adrenalin do you think was present in the suprarenal cortex involved here?

A. I don't know. I didn't assay that solution.

Q. What smooth muscle do you refer to when you state that you have noted that adrenalin relaxes it?

A. I know it does on certain of the viscera of animals, such as the large and small intestine, which is a smooth muscle of the same general shape that the uterus is. I know that it will do that with rabbits or guinea pigs. There apparently is no species difference.

(Testimony of Roland N. Icke)

Q. Adrenalin is also used a great deal for heart conditions, is it not? A. Yes.

Q. And then it comes in a form whereby the product definitely states that it is adrenalin, doesn't it?

A. I believe so.

Q. You would not expect to buy adrenalin for a heart condition where it was labeled "suprarenal cortex," would you? A. No.

Q. In fact you would not be even looking for any adrenalin if the designation was "suprarenal cortex," would [250] you?

A. It is inherent in the preparation of suprarenal cortex that there will be adrenalin with it.

Q. Do you happen to know where a product such as—aren't these things such as whole ovarian and posterior pituitary and a product such as this Indoform—do you happen to know what that is used for? Is that not used for women for some of their troubles?

A. I don't know definitely what use it has. I just know that the doctors ask for it; so apparently there must be some value. And I know that there has been no advertising and no attempt to sell it in the laboratory, other than just to act like a pharmacist in fulfilling the doctors' orders.

Q. I see. Doctor, yesterday you were testifying that Vitamin B-1 or thiamine hydrochloride does deteriorate under certain adverse conditions such as excessive heat; isn't that correct? A. Yes.

Q. And will deteriorate so to what extent?

A. If I may refer to some notes that I have?

Q. Under what?

(Testimony of Roland N. Icke)

The Witness: I would like to refer to some notes.

The Court: You may. If it is necessary, you may step down and get them.

The Witness: Thank you. [251]

A. The extent to which Vitamin B-1 deteriorates with heat depends both upon the temperature and the pH. I have—

Q. May we assume or will you tell me whether the pH. in Pluri-B—well, refering to Government's Exhibit 7—whether or not in your opinion was not the pH. proper in that instance when it was manufactured?

A. Yes.

Q. And then if that continued on without the introduction of any foreign substance into that vial, the cap was not removed, in your opinion pH. should have continued below 7, shouldn't it?

A. If there were nothing else to interfere; yes.

Q. Light would not affect it, would it, the pH.?

A. I would not expect it to. I don't know of any.

Q. And normal heat would not affect it, would it, room temperature and such as that—the pH. I mean?

A. I would not expect it to.

Q. All right. Now, what, then, is destructive of this Vitamin B-1, this thiamine hydrochloride?

A. Anything which might have been introduced into the bottle in the course of use.

Q. Well, these means that you testified about yesterday, about the alcohol or the sulfites or air that might have gotten in from puncturing the rubber cap, is that correct? A. Yes. [253]

(Testimony of Roland N. Icke)

Q. But if that did not occur, you would not expect a deterioration of the B-1, would you?

A. I would expect the B-1 to retain its potency if there were no external reasons.

Q. You would not expect within a few months for it to lose its potency up to 30 per cent, would you?

A. No; under normal conditions.

Q. And you heard Chemist Capps' testimony and, I think, subscribed to his views that the test that he gave to ascertain the quantity of B-1 was the approved test, did you not?

A. He was the one that described the dark room test, was he?

Q. Yes; I think it was fluoroscopic, was it not? Thiachrome test. I was not acquainted with the term.

A. The thiachrome.

Q. Thiachrome. Thiachrome, and they went through some color arrangement. Thiachrome tests, yes.

A. I believe that when the thiachrome test is carried out properly that it is a fair measure for Vitamin B-1 potency.

Q. I would like to call to your attention—you are acquainted with the Supplement to the Twelfth Edition of the Pharmacopoeia, a little bound booklet which I have here, are you not? [254]

A. To some extent.

Q. You know that this is a standard work, is it not?

A. Yes.

Q. And is an authority and is well accepted among your field and the medical field and among druggists, is it not? A. It is regularly accepted.

(Testimony of Roland N. Icke)

Q. Read with me. You note that I am reading from pages 82, 83:

"Thiachrome assay for thiamine hydrochloride." That is for B-1, is it? A. Yes.

Q. Let us read down here at the bottom:

"After preparation of assay solution, the amount of material taken for the assay should be such that the ratio of the volume of tenth normal sulphuric acid used for the extractive amount of sample is at least 15 to 1 and the content of thiamin equivalent to 30 to 100 micograms of thiamine hydrochloride."

Now, I want you to note this next sentence:

"Place the accurately-weighed quantity of material to be assayed in 65 cc's of tenth normal sulphuric acid contained in 100 cc's centrifuge tube and digest it an a steam bath with frequent mixings for 30 minutes." Do you note that? [255] A. Yes.

Q. It says, "for 30 minutes" that that thiamine hydrochloride is to be placed on a steam bath. Does that not mean that activated hot steam is actually flowing up against the tube in which that is and reaches almost a boiling point?

A. That is true. But the pH. of that strong sulphuric acid would be down around 1. The lower edge is an extremely low pH. and you would not expect the thiamin to be not stable at a very low pH.

Q. Isn't the product in here such to keep at around 3, didn't you say on your opening testimony?

A. Yes.

(Testimony of Roland N. Icke)

Q. And that is rather low and one that you would expect to stay stable, too, as compared to 7, isn't it?

A. Yes; but it would be less stable than it would at a pH. of 1.

Q. But I ask you if that steam would not almost constitute a boiling condition; isn't that correct?

A. Yes.

Q. And that also states to keep it on that for 30 minutes, doesn't it? A. Yes.

Q. And while that process is going on the product is subjected to oxidation from air getting in about it; isn't [256] that true?

A. I would like to see that again, please?

Q. Well, you do not enclose the product while the steam is flowing upon it and you are assaying it, do you? The part that I have marked here at the bottom. (Referring to book.)

A. This was done in a centrifuge tube, so apparently it was open to the air.

Q. And that is a more adverse condition, with a revolving or with a full allowance of air, than occurs in a vial of the character of one of these, is it not?

A. I do not believe that that is revolving during that time.

Q. Well, at least, these do keep out air, do they not, these vials? A. Yes.

Q. Such as the one I have in my hand?

A. Yes.

Q. So, then, you would expect the Vitamin B content or the thiamine hydrochloride to stand up in a closed vial after six months, and retain the potency or practically the potency that was reflected from the label, if

(Testimony of Roland N. Icke)

it did have that amount when the label was placed on it, would you not?

A. I would if nothing else had affected it.

Q. Now, I would like to ask you something. Epinephrin [257] is another word for adrenalin, is it not?

A. Epinephrin.

Q. Epinephrin. And you are acquainted with the work, a Manual of Pharmacology by Solomon, are you not? A. Yes.

Q. And the Fifth Edition, is that correct?

A. Yes.

Q. And it is a recognized authority in its field, is it not? A. Yes.

Q. A standard work, I mean. Is it correct that whenever I use the word "epinephrin" that I could also be using the word "adrenalin"?

A. That is correct.

* * * * * * * * *

Q. "Reversal of adrenalin"—while the word here is "epinephrin"—"inhibition by pituitary extract. The uteri of guinea pigs and non-pregnant rats are ordinarily relaxed by epinephrin or adrenalin." That is what you stated just a while ago? A. Yes.

Q. "If, however, they are first treated with pituitary [258] solution, the epinephrin or adrenalin produces contraction." Do you subscribe to that? A. Yes.

Q. "The diffrence in the normal resistance of different uteri to epinephrin may, therefore, depend on the content of pituitary. This sensitizing action seems to be in the

(Testimony of Roland N. Icke)

peripheral nervous mechanism and not in the muscle itself." Do you subscribe to that statement or doctrine?

A. That is correct; but I believe you have brought out the wrong implication.

* * * * * * * * *

Mr. Stick: Pardon me, please, your Honor.

Mr. Neukom: I beg pardon.

Mr. Stick: I think he wanted to make an explanation of that answer.

The Court: He may.

A. This says: "If, however, they are first treated with pituitary solution, the epinephrin produces contraction." It does not say that if they are simultaneously treated with posterior pituitary and epinephrin, that contraction will take place.

Q. By Mr. Neukom: Didn't you hear Chemist Mason state that that is just what he did? He treated this [259] substance with pituitary first.

A. But he did not add epinephrin to it.

Q. But you say epinephrin was present in this suprarenal cortex.

A. There is quite a difference there. After his test 1-B, that test smooth muscle was washed so as to remove all of the posterior pituitary. That is shown by the fact that the record of the contraction came back to normal; so that there was no posterior pituitary there, and that it was in a condition the same as if no posterior pituitary had been added at all. That is further verified by the fact that the record of 3-B is essentially that of 1-B.

Q. Doctor, didn't you state that this amount of adrenalin or epinephrin in the suprarenal cortex, while

(Testimony of Roland N. Icke)

you did not know whether it was there or not, it could be in such a small amount it would still have an effect? Now, would the washing remove even that small quantity also? A. Yes.

Q. In other words, it would be present to retard this test, according to your opinion, upon your surmise that it is present in suprarenal cortex, is that it?

A. I know it is present in suprarenal cortex.

Q. But yet the label says nothing about its presence; isn't that correct? A. That is correct. [260]

Q. Doctor, is it not true that the public today buy bread with Vitamin B-1 placed in it and that the enriched flour, so enriched, retains its potency even after the baking of the bread?

A. That is true, but there is a difference between a solution and the material in the relatively dry form. A solution is more susceptible to change than the dry material.

Q. Don't they have to mix that up and heat it up with the dough in order to form the bread?

A. Yes.

* * * * * * * * *

Q. And it has to be dissolved; it is not just a mere powder in there, is it? A. No.

Q. Doctor, isn't it likewise true that your cereals which are placed in ovens, they have added B-1 or thiamine hydrochloride to them and they come out and they are potent?

A. They are potent, but I know that an excess is added above the amount claimed for that product, because the manufacturers expect a certain amount of loss.

(Testimony of Roland N. Icke)

Q. You really, actually, Doctor, feel that this Pluri-B product that your employer puts out is a pretty stable product; it is not a fragile product, is it?

A. It is intended to be stable. [261]

Q. And you would be highly surprised if within a few months after its manufacture, it was 30 per cent off, wouldn't you?

A. If nothing had happened to it, I would be surprised.

Mr. Neukom: That is all.

Mr. Stick: That is all.

The Court: I have two or three questions of the doctor. Doctor, taking up, first, this Vitamin D (in oil).

The Witness: Yes, sir.

The Court: What would have to happen to that solution to reduce the potency from a half million units per cubic centimeter of Vitamin B down to 350,000, in your opinion?

The Witness: In my opinion, some oxidizing agent would have to have been added to that for the potency to decrease.

The Court: Can you illustrate to what extent an oxidizing agent would have to be introduced into the solution and how it might be done? Would it have to be done intentionally?

The Witness: No; it would not have to be done intentionally.

The Court: Could it be done by use of the doctor in perforating the rubber cork with a hypodermic needle containing a sterilizing solution such as you referred to yesterday?

(Testimony of Roland N. Icke)

The Witness: Yes; it could very readily be done that way without the doctor's realizing that it was being done.

The Court: Well, would one such injection of a hypo- [262] dermic needle carry it out or would it require, likely, repeated use?

The Witness: It would only take one to cause some destruction. It would be impossible to say without knowing just how much of the oxidizing agent was added and at what temperatures the materials were kept.

The Court: Suppose the doctor did, as I believe you described, puts his needle in some alcohol and shakes it off and squirts it out, and puts the needle into the rubber cork, would such a process as that likely introduce an oxidizing agent that would reduce the potency of the contents of the bottle by several thousand units?

The Witness. It would reduce the potency some. I have no way of knowing just how much it would reduce it.

The Court: But if you assume that here was a product, Vitamin D (in oil), manufactured with a potency of 500,000 units of Vitamin D per cubic centimeter, and six months later, say, was found to have only 350,000; if you assume that, if the only use had been made of it had been the injection of the doctor's hypodermic for the purpose of extracting the solution from the bottle, would you assume that there had been many such applications of the hypodermic?

The Witness: Probably so.

The Court: And would you assume there had been extremely careless use, shall I say, by the doctor? [263]

The Witness: No; I do not believe I would call it careless. So far as I know, it has not been called to

(Testimony of Roland N. Icke)

the doctors' attention that there are oxidizing agents in isopropyl alcohol.

The Court: Assume if the doctor picked up his hypodermic and puts it in isopropyl alcohol, and supposing he tries to be real careful and shakes it and manipulates the needle two or three times, the syringe part of it, in an attempt to clear the container of any foreign substance at all, and then wipes it off, he can't wipe out the interior of the needle, can he?

The Witness: No; nor the syringe.

The Court: Yes. So if he injects that, inserts it through the rubber cork, he is likely, in your opinion, greatly to decrease the potency of the next injection?

The Witness: I believe it is quite possible and very likely that it would reduce the potency.

The Court: Considerably?

The Witness: Yes.

The Court: How many hypodermic injections in the normal use of Vitamin D for such a purpose could be expected from this bottle which is Exhibit A?

The Witness: Is that a 30 cc vial?

The Court: I am sure I can't tell you. It is not labeled, I think. Would you like to examine it closer?

Mr. Clerk, will you hand it to the witness? [264]

The Witness: This is a 15 cc vial.

The Court: Approximately how many hypodermic injections could a doctor procure of Vitamin D from that vial?

The Witness: From 15 to 30.

The Court: From 15 to 30. The patient who might be No. 28, in your opinion, would likely get a practically useless injection, wouldn't he?

(Testimony of Roland N. Icke)

The Witness: The amounts of material which he would undoubtedly put into the bottle would vary considerable with how many times he moved the plunger back and just how dry the needle and syringe became by that process; so that it would be extremely variable.

The Court: Yes; I understand. But I am assuming the normal process that we have been describing, of a doctor who tries to be careful but who cannot be so meticulous as to bake his hypodermic dry each time before he inserts the needle into the solution.

The Witness: The last doses would be considerably less potent than the first.

* * * * * * * * *

The Court: I want to turn now to this one or two counts with respect to Pluri-B. Pluri-B for intramuscular use con- [265] tains, acording to the label, one milligram of riboflavin. Is that, in your opinion, coupled with the other ingredients, sufficient for the purpose for which Pluri-B is intended?

The Witness: The opinion of the medical doctor who uses that varies considerably. Some of the doctors want even more riboflavin and some others, less. It is a matter of their own opinion. I would not be qualified to say.

The Court: I am asking your opinion, not the doctor's opinion.

The Witness: I see.

The Court: In your opinion, this product, Pluri-B, containing one milligram of riboflavin is sufficient for the purpose for which it was intended?

The Witness: Yes.

(Testimony of Roland N. Icke)

The Court: And it is marked "for intramuscular use." It is sufficiently potent, in your opinion, with respect to riboflavin, is that correct?

The Witness: Yes, sir.

The Court: Can you tell me why the same product, Pluri-B, which is intended not only for intramuscular, but also for intravenous use, contains two milligrams, twice the amount?

The Witness: I know that some of the other manufacturers have prepared more concentrated solutions, that is, solutions containing more riboflavin; and that the laboratory had received requests for B Complex solutions which had more [266] riboflavin in it that the one milligram.

The Court: What I am getting at, do you know of any reason why the stronger solution should be marked for intravenous as well as intramuscular use, whereas the solution that is intended for intramuscular use only is the weaker solution insofar as riboflavin is concerned?

The Witness: I do not believe that the riboflavin content there would make any difference whether it would be used intravenously or intramuscularly.

The Court: Would it be erroneous to assume that a solution that has one milligram per cubic centimeter of riboflavin, that the riboflavin in such a solution would be less likely to precipitate than a similar solution or a like solution containing twice as much riboflavin per cubic centimeter?

The Witness: If the other ingredients in there were the same, it probably would be less likely to precipitate.

The Court: That is our assumption, is it not?

The Witness: Yes.

(Testimony of Roland N. Icke)

The Court: The Pluri-B that we are referring to is identical, except that the one marked for intramuscular or intravenous use has twice as much riboflavin as the solution which is marked for intramuscular injection only.

The Witness: Yes.

The Court: That is all I have. [267]

Mr. Neukom: I just wanted to ask, since you brought up a subject.

Q. Doctor, if a needle is sterilized in a steam cabinet, there would therefore be removed any oxidizing agent, would there not?

A. I suppose so. If the oxidizing agent is water-soluble, I think that would be removed.

Q. Now, Doctor, don't you know—you have talked about oxidizing agents here and you have told the court where you think they may come from. Is it true, Doctor, that this sterilization process of the little baths, the very chambers that the doctors have will actually sterilize the needle and leave no oxidation agent on the needle?

A. Not all oxidizing agents are water-soluble. I don't know about the oxidizing agent in isopropyl alcohol, whether it is soluble or not; so I could not say whether the steam treatment would remove it.

Q. Now, Doctor, most medical men have this little needle which fits onto a sort of a glass tube, that they can see how much they are drawing in, don't they, from the plunger? A. Yes; they observe the solution.

Q. Isn't it true that about 80 to 90 per cent of the physicians have that needle removed and that needle is placed in a boiling bath of water, thoroughly sterilized before it is used to obtain any of these solutions to inject into people; [268] isn't that true?

(Testimony of Roland N. Icke)

A. I know that a great many doctors do. I don't know what the percentage is. I know some of them do not use that process; they use isopropyl alcohol or mercuricides almost exclusively.

Q. If the doctor did use the first process, the sterilization process, you would not believe that there should be any oxidizing agent to any extent that you have stated might affect the product, do you?

A. If he had not previously used a material in which some water-insoluble oxidizing agent had got on the material, I would agree with you.

Q. What if he had previously used isopropyl alcohol and then steamed and sterilized his instrument; would you state that that alcohol would still remain there in an amount of sufficient oxidizing agent to affect this Vitamin B?

A. It is not the alcohol that is an oxidizing agent. The peroxides are dissolved in the alcohol, and I don't know whether the peroxides are soluble in water or not; so I couldn't say whether they would be removed.

Q. Doctor, you have never actually performed tests where you have taken a hypodermic needle, stuck it in some alcohol, shook it dry, allowed the volatile alcohol to go off, then insert it in one of these bottles, draw out repeatedly, and then determined how much potency had been [269] lost as a result of, say, 10 or 12 such tests?

A. No.

* * * * * * * * *

The Court: That is all, Doctor.

Mr. Stick: Defendants rest.

Mr. Neukom: I would recall Dr. Tolle just for a few more questions, your Honor.

PLAINTIFF'S CASE IN REBUTTAL

CHESTER D. TOLLE,

recalled as a witness in rebuttal by plaintiff, being previously sworn, was examined and testified as follows:

Direct Examination

By Mr. Neukom: [270]

* * * * * * * * *

Q. Before going on that, you were in charge of the office for a certain branch of the files in the office of the Food and Drug, were you not?

A. I received all samples.

Q. And you had occasion to receive this sample that Chemist Capps—I have allowed him to go, your Honor—you had occasion to first receive that, did you not?

A. I did.

Q. And that is Government's Exhibit 7, I believe—Government's Exhibit 6, the Pluri-B. When that was received in this vial that has been testified to here, did you have occasion to observe whether or not that vial when received appeared to be full and appeared to be not tampered with? A. It did.

Q. Appeared to be in the state of a new vial, is that correct? A. That is correct.

Q. And you passed it on to the other analyst after analysis? A. That is correct. [271]

Cross Examination

By Mr. Stick:

Q. Dr. Tolle, have you ever run any experiments at all [272] with reference to tests of an oxidizing agent

(Testimony of Chester D. Tolle)

getitng into a bottle containing Vitamin D by the use of a hypodermic needle?

A. No; because that has not been of interest to me.

Q. You have not run any tests and have no knowledge from the experience of a test on that point?

A. You are quite right. I would like to explain my answer, if I may.

The Court: You may.

A. In the case of the products that we examine, we do not have occasion to examine bottles that have been opened, because I see all the records as they come in with the sample and, had a sample been opened the record would so indicate and then we would not make a test on it in our laboratory. That is one thing that is an unwritten law with the inspectors, according to my opinion and according to advice I have heard given to them, that they make known whether or not a sample that has been picked up has been taken out of the container.

Q. By Mr. Stick: Now, you say they make that known. How do they make that known?

A. By a note on the collection record.

Q. And that note says that they have not opened it?

A. No; it does not say that they haven't opened it.

Q. What does it say?

A. If it has been opened, it so states; and then they [273] have an affidavit from the doctor or the pharmacist or whoever may have indicated that he has opened it.

Mr. Stick: Your Honor, there being no testimony before of such thing in either of these instances, any surmise on his part would be purely hearsay as to a test, that it had been opened.

(Testimony of Chester D. Tolle)

The Court: That is a matter of argument. He has merely said in effect that the inspector is to report that he has been informed that this bottle had not been opened.

Q. By Mr. Stick: Did you ever see any of these bottles before they arrived in your hands in Washington on some particular day that you have testified to?

A. I did not.

Q. You do not know, of your own knowledge, when they were shipped? A. I do not.

Q. Or, of your own knowledge, to whom they were shipped? A. I do not.

Q. Or, to your own knowledge, what happened to them when they were received by the consignee of the shipment? A. Certainly not.

Q. Of your own knowledge, you have no knowledge as to what was in the bottles at the time they were shipped? A. No.

Q. All you know about it is that at the time it came to [274] you in Washington it appeared to be an unopened bottle and one that had not been used?

A. That is right.

Mr. Stick: That is all.

Redirect Examination

By Mr. Neukom:

Q. You do know what you found from your analysis?

A. That is right.

Q. And you have heretofore testified to that?

A. I have.

Mr. Neukom: That is all. [275]

* * * * * * * * *

Mr. Neukom: Mr. Mason.

ARNOLD E. MASON,

recalled as a witness in rebuttal by the plaintiff, having been previously sworn, was examined and testified as follows:

Direct Examination

By Mr. Neukom:

Q. With respect to the vial designated as 3 which you, and then, later, Mr. Buell analyzed and which is in [276] support of Count I, will you tell the court the condition of the contents of that vial and the apparent condition of the sealer or cork when you first received it in conjunction with your duties?

A. The vial was full and the rubber stopper or cork was protected, with a celluloid seal around it when I received it. It appeared as if it had never been opened.

Q. Will you just tell the court once more with regard to this subject matter, now, of adrenalin or epinephrin? Will you tell the court just what you did with regard to first washing the uterus horn with the pituitary standard solution?

A. The uterine horn is allowed to relax to a constant level before the assay is ever begun, then a standard solution of posterior pituitary is added to that bath, the muscle is caused to contract by that pituitary solution. When it contracts to a maximum for the given amount of standard pituitary given to it, the bath is washed out and clean, fresh, aerated bathing fluid is again surrounding the muscle. The muscle relaxes to its normal level again and that procedure is either repeated or an amount of sample is added to the bath.

The Court: In this case, after you washed out, shall I say, the bath from the first test with the standard

(Testimony of Arnold E. Mason)

solution, you applied to it the solution under investigation?

The Witness: The solution under investigation was then added in 2-B on the board. [277]

* * * * * * * * *

Q. Mr. Mason, are you acquainted with the properties of the adrenalin gland?

A. Yes. I have performed assays on adrenalin solutions for the Food and Drug Administration for over three years.

Q. And the adrenalin gland is composed of two parts, is it?

A. It is composed of the adrenal medulla and cortex.

Q. And does the cortex itself contain adrenalin?

A. The cortex might contain very small amounts of adrenalin. The main hormone of the cortex is its own hormone.

Q. From your experience and from your studies do you have an opinion as to whether or not suprarenal cortex, 30 grains, as is indicated on this product here, Indoform, contains sufficient adrenalin to make it impossible to test posterior pituitary that you were testing for in this test?

A. That would depend upon what form the suprarenal cortex was in and under what conditions it was put into solution and upon how much adrenalin was present originally in the gland—in the cortex of the gland. [278]

(Testimony of Arnold E. Mason)

Q. In this particular instance here what is your opinion, bearing in mind what you have testified to, to explain now as to the existence or lack of existence of posterior pituitary in those products mentioned?

* * * * * * * * *

A. As I have stated before, there is little or no posterior pituitary in that product from the results of my test.

Q. Do you think your test was equally as effective or non-effective by the fact that this product had in it suprarenal cortex or will you explain?

A. I believe the test was as effective as if suprarenal cortex had not been there. I have had occasion to assay many other preparations of similar nature, glandular preparations, and the amount of posterior pituitary that is claimed can be assayed for and proved to be present in the presence of other glandular preparations and suprerenal cortex.

Q. In the presence of suprarenal cortex? Is that correct? A. Yes, sir.

Mr. Neukom: That is all.

The Court: Do you agree that the presence of a quantity [279] of adrenalin or epinephrin in the suprarenal cortex, constant in the liquid, would tend to negative the test you made for the presence of posterior pituitary in the solution?

The Witness: No, your Honor; I do not. Under the conditions of this test the bath in which the guinea pig uterus is suspended is being constantly aerated with oxygen. It is commonly known that adrenalin is very unstable in air, and also that adrenalin is very short

(Testimony of Arnold E. Mason)

acting, that is, it will act for a short time, because it is dissipated both by the tissue and by air oxidation. Posterior pituitary, on the other hand, is quite a long acting drug. I think, first, that the adrenalin, if it was present, would have been destroyed so rapidly that it would not have interfered with the test.

The Court: Would the treatment of the uterine muscle with the standard solution of posterior pituitary which you made in the first test, would that carry over after the bathing of the muscle preparatory to the second test, so as to prevent the presence of any adrenalin from interfering, or would the bath negative the first application of posterior pituitary for that purpose? I am referring now to the text which was read here to Dr. Icke, in which the author stated, as I recall it, in substance, that the treatment of the muscle with posterior pituitary would prevent the interference by the epinephrin or adrenalin.

The Witness: I don't know what the author of the text [280] means by pre-treating with posterior pituitary. If he means he adds pituitary preparation to a uterine muscle and lets that pituitary stay in solution, then adds the adrenalin, he must be very careful of the amount of pituitary that he adds, in order to prove his point; for if he is not, the muscle will contract to a maximum and he will never be able to say that adrenalin would enhance the pituitary contraction or it would reverse itself and cause a contraction. It seems to me that he must have pre-treated the muscle in a manner such as this, then washed the solution out and immediately added epinephrin.

The Court: In other words, washed the muscle just as you did upon the completion of the first test?

(Testimony of Arnold E. Mason)

The Witness: Yes. There is a great species difference, as can be cited in the literature, in the action of adrenalin on uterine muscles—not only on smooth muscles, but even on uterine muscles. It will act different in different species; and just exactly what the author means in his text I can only surmise; and that is, that he does not mean that he keeps the pituitary in the solution and adds the adrenalin on top of it.

The Court: If you assumed that, by reason of the presence of suprarenal cortex in this solution of Indoform which you were testing, some epinephrin or adrenalin was present, would you feel that you should make some allowance for that fact [281] in your conclusions?

The Witness: Do you mean in this test?

The Court: Yes.

The Witness: Under the conditions under which I was running tests, I would not feel I should make any allowance unless that fact was so stated on the label.

The Court: Irrespective of what the label said, if we assume—I am asking you to assume, now?

The Witness: Assume that adrenalin—

The Court: That it was present by reason of the presence of the suprarenal cortex in that solution; and if you so assume, would that alter your conclusions as to the accuracy of your test?

The Witness: Not as to the accuracy of my test.

The Court: Would it alter your conclusion which you have stated as to the presence or absence of posterior pituitary in that solution?

The Witness: No, sir. I am sorry I misunderstood your question in the first place.

The Court: That is all I have.

(Testimony of Arnold E. Mason)

Mr. Neukom: I might ask him this one question, your Honor:

Q. Does the viscera and the uterine muscle all react the same with the same stimulus?

A. No, sir. [282]

Q. Explain.

A. As I explained a moment ago, there is a difference in the way viscera and uteri will act in different animals. There is even a difference in the way the uterine muscle itself will act in different animals. For example, adrenalin may contract the uteri of some animals; it may relax the uteri of other animals. There is no hard and set rule. It depends upon the animal. The only way that that can be proven is by investigation. The only way the action of a drug can be shown is by investigation.

The Court: What animal did you use the uterus of here?

The Witness: A guinea pig.

The Court: What is the effect of adrenalin upon the uterus of the guinea pig?

The Witness: In normal guinea pigs, adrenalin by itself will relax the muscle.

The Court: This was a normal guinea pig that you used?

The Witness: A guinea pig prescribed in the test.

The Court: So you would assume, would you, that if the adrenalin was present in the solution, that the tendency of that adrenalin as present would be to relax the muscle, and hence to counteract the tendency to contract?

(Testimony of Arnold E. Mason)

The Witness: Not if pituitary solution was also present. [283]

* * * * * * * * *

The Court: By that, do you mean that the presence of pituitary would tend to negative the presence of the adrenalin, and vice versa?

The Witness: You are assuming that adrenalin is present in this solution?

The Court: Yes. I have not assumed any quantity.

The Witness: It would depend both upon the quantity of both adrenalin and pituitary.

The Court: Yes. So if there were an "X" quantity of adrenalin, it might be a stand-off so far as the effect on the muscle is concerned with "Y" quantity of pituitary, is that correct?

The Witness: Do you mean with an amount of adrenalin present in that solution might inhibit any action of the pituitary?

The Court: Inhibit the action of the muscle, might it not?

The Witness: To pituitary?

The Court: In other words, if there is a quantity of adrenalin in the solution which, as I understand it, you would say in a normal situation would tend to relax that muscle?

The Witness: Yes, sir. [284]

The Court: Here is an unknown quantity of posterior pituitary which, as I understand it, would tend to contract the muscle?

The Witness: That is right.

(Testimony of Arnold E. Mason)

The Court: If that adrenalin were present, before you could measure the presence of posterior pituitary by the muscular contraction, there would have to be enough to overcome whatever counter-effect the adrenalin would have, would there not?

The Witness: It would have to be enough. But, according to the text that was read in court a while ago, in the presence of pituitary the epinephrin relaxation would be reversed.

The Court: You mean by that, is it your understanding that the presence of adrenalin or epinephrin and pituitary in the same solution would convert the epinephrin into a contracting agent on the muscles instead of a relaxing agent?

The Witness: I would assume that that is what would happen.

The Court: That is all I have.

Mr. Neukom: May the witness just read that paragraph, your Honor? He was not present or close when this was being read, and he might want to make an explanation. I will not read it into the record here.

Q. After having read that, do you wish to make any [285] additional explanation to the court to clarify your position?

A. No. I again state that I think that the adrenalin in this sample under investigation, if it was present, definitely would not have interfered with any assay for posterior pituitary.

The Court: Why do you say that? Why would that be so?

The Witness: I have examined a number of other samples, as I have stated, glandular substances very simi-

(Testimony of Arnold E. Mason)

lar in nature to the one under investigation. I have examined them for labeled contents of posterior pituitary. There are other similar samples which claim three international units per cubic centimeter of posterior pituitary on the label, also containing these other glandular constituents. And they can be assayed and it can be shown that the amount of posterior pituitary present is 100 per cent of the labeled potency.

The Court: Irrespective of the presence—

The Witness: Irrespective of the presence of suprarenal cortex. I will not say "adrenalin", since we are assuming that adrenalin is in this product. We have no proof of it.

The Court: So, irrespective of the presence of adrenalin?

The Witness: Irrespective of the presence or absence of adrenalin, those assays were still carried out and it was shown that the labeled content of posterior pituitary was [286] present.

The Court: Doesn't that make a question; there might have been more than three, might there not, in that solution that you are referring to? Now, might there not have been enough posterior pituitary, first, to overcome whatever counter-effect or relaxing effect the adrenalin present might have had, plus the three units?

The Witness: The assay showed the presence of only three units per cubic centimeter.

The Court: Yes. But the assay was the same type of assay you made here?

The Witness: Yes, sir.

The Court: And might there not have been, in order for you to reach that result—

(Testimony of Arnold E. Mason)

The Witness: More than that?

The Court: There was three units plus enough neutralizing counter-effect of the quantity of epinephrin present?

The Witness: If any excess was present— I don't believe I can answer that question.

The Court: How can you know, if you start out with the supposition that the presence of epinephrin would tend to neutralize the pituitary present, how could you ever know how much pituitary was present unless you did something about the adrenalin that might be present?

The Witness: The only way you could know how much was [287] present, as I said, is to assay it.

The Court: I am only interested in the end result here. Our problem is to determine whether this pituitary is present; and if so, in what quantity. Isn't that our problem?

The Witness: Yes. The only way that could be determined is by an assay for the presence of posterior pituitary.

The Court: It could not be determined by the test you made?

The Witness: That test I made is not what one might call an assay, because it is impossible to get an assay with the product under investigation. In the official United States Pharmacopoeia there is an assay for posterior pituitary which starts in this manner. However, the sample being investigated must cause a contraction of the muscle as great as the standard solution when one is given following the other for four doses, then a fifth dose of standard solution must be given, which is 25 per cent higher than the other two doses of the

(Testimony of Arnold E. Mason)

standard solution, to show that the muscle has not ben contracting at a maximum all that time; in other words, that it could have gone higher if it wanted to; that the preparation under investigation was not actually 150 per cent of what you were testing it for, but that the contraction went up only as high as the standard and, if given in amounts equivalent to that of the standard solution, it therefore would have the same strength of the standard, and [288] if that was made up according to the labeled potency, it would be 100 per cent.

The Court: Have you made any test to determine the relative quantity of epinephrin present in a given amount of suprarenal cortex?

The Witness: No, sir.

The Court: That is all I have.

Q. By Mr. Neukom: Do you know whether epinephrin does, though, rapidly oxidize and pass away under tests such as you have made?

A. Very rapidly. It is rapidly oxidized in the air, and in a test like this, as I stated, there is oxygen bubbling through the bath to aerate the muscle, and that oxygen present would rapidly destroy minute amounts of adrenalin.

The Court: Would you assume that there would be minute amounts where the quantity of suprarenal cortex present is 30 grains per cubic centimeter?

The Witness: Very minute amounts, if any.

The Court: How would you know that?

The Witness: The only way you could know whether any amount of adrenalin was present would be to test the preparation for adrenalin. [289]

* * * * * * * * *

Mr. Neukom: Dr. Wiley for just a couple of questions, if your Honor pleases.

FRANK H. WILEY

called as a witness in rebuttal by plaintiff, having been previously sworn, was examined and testified as follows:

Direct Examination

By Mr. Neukom:

Q. Dr. Wiley, when you received Government's Exhibit No. 1 there was in all how many vials?

A. Six vials.

Q. And of the two that have been produced here, did they appear to be sealed, capped and full?

A. They did. All six of the vials, as a matter of fact, were full. [290]

* * * * * * * * *

Q. By Mr. Neukom: Did all six of the vials appear to have a percentage of undissolved particles such as the one that is a part of Government's Exhibit No. 1?

A. They did.

Q. Did you endeavor to pass these vials into a lukewarm bath to ascertain whether or not the dissolved particles would become saturated?

A. I did. That is a part of the general routine in examining products of this type in the laboratory. We first examine the product while the label is still on the vial, if that is at all possible. Sometimes the label covers up so much of the vial that it is almost impossible to see the contents. But where we can see them on any portion of them, we examine the material for undissolved particles. Then, to make a more complete inspection, the vials are placed in warm water which runs around 150

(Testimony of Frank H. Wiley)

degrees Fahrenheit and are allowed to remain in there for a period of time of about 10 to 15 minutes. During that time the labels are loosened from the vials and float off. The vials are then dried and the contents re-examined.

In this particular case the undissolved material was still present although the solution in these vials was quite warm. [291]

Q. While this was not a matter that you testified to, I forgot to ask it of Dr. Tolle. Is it not true that thiamine hydrochloride or the B-1's and the complexes are, in addition to being a food, also in a classification of a drug?

A. Yes; they are so classed. The fact that thiamine hydrochloride appears in the U. S. Pharmacopoeia makes it a drug under the Food and Drug and Cosmetic Act.

Mr. Neukom: That is all.

The Court: In picking up these samples does the Administration pay the person who has the samples for them?

The Witness: We always offer to make payment. Sometimes that is not required, but ordinarily it is required and we make whatever payment is necessary for the samples.

* * * * * * * * *

Mr. Neukom: The Government rests now, your Honor.

The Court: Do both sides rest?

Mr. Stick: Yes, your Honor. [292]

* * * * * * * * *

Arguments were made on behalf of the parties and the matter submitted to the Court.

* * * * * * * * *

The Court: The court finds the defendants guilty as charged in Count I of the Information; and guilty as charged in Count II; guilty as charged in Count III; guilty as charged in Count IV; not guilty as charged in Count V; not guilty as charged in Count VI; and guilty as charged in Count VII of the Information.

Guilty as to all counts other than V and VI, and not guilty as to Counts V and VI. [342]

[Endorsed]: Filed Aug. 11, 1947. [343]

[Endorsed]: No. 11690. United States Circuit Court of Appeals for the Ninth Circuit. Pasadena Research Laboratories, Inc., a corporation, and Russell R. Bavouset, Appellants, vs. United States of America, Appellee. Transcript of Record. Upon Appeals From the District Court of the United States for the Southern District of California, Central Division.

Filed August 23, 1947.

PAUL P. O'BRIEN,

Clerk of the United States Circuit Court of Appeals for the Ninth Circuit.

In the United States Circuit Court of Appeals
for the Ninth Circuit

No. 11,690

PASADENA RESEARCH LABORATORIES, INC., a corporation, and RUSSELL R. BAVOUSET, an individual,

Appellants,

vs.

UNITED STATES OF AMERICA,

Appellee.

STATEMENT OF POINTS WHICH APPELLANTS INTEND TO RELY ON THE APPEAL, PURSUANT TO RULE 19(6) OF THIS COURT

On appeal, Defendants-Appellants intend to rely on the following points in support of their appeal:

I.

The District Court erred in overruling defendants' objection to the latter of the following questions propounded to the witness Wiley:

> "Q. By Mr. Neukom: Dr. Wiley, taking the two vials, part of Government's Exhibit No. 1, which I understand you examined about six weeks after the shipment in question here, from your knowledge of sterile solutions and from your observation of sterile solutions, your experience, are you able to express an opinion to this court as to whether or not the contents of those two vials, Government's Exhibit 1, did contain the undissolved particles you noticed there then as of the date they were shipped,

namely, on or about June 18, 1946? Your answer is yes or no."

* * * * * * * *

"Q. By Mr. Neukom: Will you please relate your opinion?" (Reporter's Transcript of Proceedings, page 17, lines 9 to 18, and page 18, lines 17 and 18.)

II.

The District Court erred in overruling defendants' objections to the following questions put to the witness Mason:

"Q. Assuming, Mr. Mason, that this product was not exposed to excessive temperatures, that is to say, that you said was 212 degrees is the destructive temperature; and assuming the product was handled in a normal and careful manner, retained in the bottle, as Government's Exhibit No. 4, I believe; assuming which bottle you opened and conducted the tests as you have testified; and, with the assumption of what you found or did not find at that time, have you an opinion as to whether or not this product contained three international units of posterior pituitary on September 17, 1945?"

* * * * * * * *

"Q. By Mr. Neukom: Now assuming that all that you have testified to here and the explanations you have given, what is your opinion, carrying on the assumptions that I have enumerated—what is your opinion as to the amount, if any, of posterior pituitary was in the product on or about September 17, 1945?" (Reporter's Transcript of Proceedings, page 61, lines 16 to 25, and page 62, lines 6 to 10.)

III.

The District Court erred in overruling defendants' objections to the following questions put to the witness Capps:

> "Q. Now, assuming that the product received ordinary and reasonable care, and was not exposed to excessive heats, such as heats any more than would be normal from shipping and the weather, and basing upon what you found on September 24, 1945, the amount of the B-1 or thiamine chloride that you found, have you an opinion as to what percentage or what amount that product, substance, or solution had on or about July 16, 1945, the date it was originally shipped?" (Reporter's Transcript of Proceedings, page 94, lines 12 to 19.)

IV.

The District Court erred in that there is no evidence in this case upon which a finding of guilty could be made against either of the defendants.

V.

The District Court erred in that the finding of guilty is contrary to law.

VI.

The District Court erred in that the finding of guilty is contrary to the weight of the evidence.

VII.

The District Court erred in that the finding of guilty is not supported by substantial evidence.

VIII.

The District Court erred in that it did not give defendants the benefit of reasonable doubt which they were legally entitled to.

IX.

The District Court erred in that the evidence in this case did not demonstrate beyond a reasonable doubt the defendants' guilt.

X.

The District Court erred in that the Government failed to eliminate the possibility of the products having lost their strength or potency through the failure or neglect of parties other than the defendants.

XI.

The District Court erred in that the Government failed to prove that heat, or light, or lack of refrigeration, or moisture did not in some way come in contact with the bottles so as to cause the alleged loss of strength.

X.

The District Court erred in entering judgment in favor of the United States, while, in fact, and law, it should have been entered in favor of the defendants.

Dated at Los Angeles, California, this 15 day of September, 1947.

JOHN C. STICK
R. WELTON WHANN
By R. Welton Whann
Attorneys for Appellants

Received copy of the within Statement this 15 day of Sept., 1947. James Carter, by N. W. Neukom, Attorney for Appellee.

[Endorsed]: Filed Sep. 18, 1947. Paul P. O'Brien, Clerk.